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ANNALS OF THE RHEUMATIC DISEASES

CONTENTS

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EDITORIAL

It is with the greatest of pleasure that we extend the hospitality of our pages to the American Rheumatism Association for a report of the Proceedings of their important reunion meeting held last year in New York. *The Annals of the Rheumatic Diseases*, although published in London, and closely affiliated with the Empire Rheumatism Council, has never adopted a policy of accepting articles only from British sources, but opens its pages to all workers in rheumatic diseases; and it is pleasant to recall that within the past year communications have been printed from Sweden, Switzerland, Brazil, Australia, and the U.S.A., as well as from workers in the British Isles. With two eminent American rheumatologists serving on the editorial committee, the link between workers on the two sides of the Atlantic has been well established for some time past, and we hope that this present issue of the *Annals* will make the link still firmer. We believe that the Proceedings of the American Rheumatism Association will be a great stimulus to British workers. The papers reflect the trend of thought in America, and suggest both research and therapeutic advances which should be followed up.

The opening address by the President, Dr. Paul Holbrook, is stimulating and points out much that needs still to be done to encourage the study of the subject and to advance the knowledge of the general practitioner in the problems presented by the manifold forms of rheumatism and the best methods of treatment. His suggestions on the formation of rheumatism societies throughout the country deserve careful consideration, and while experience of the attendance of busy practitioners at medical meetings does not promise that such societies would be easily organized and become active, it might be possible to organize rheumatism discussions, perhaps linked with the division meetings of the British Medical Association, and to form groups of practitioners disposed to interest themselves in the subject, whose observations upon their patients in the course of daily practice might prove of great value. It is not unlikely that encouragement in this direction might produce results; such groups could become affiliated with the Empire Rheumatism Council or with the Heberden Society.

Now that many who have hitherto subscribed to hospitals are tending to withdraw their subscriptions on the ground that their maintenance is to be a matter for the State, there is an opening for inducing them to devote their interest and financial support to the establishment of research fellowships in rheumatic diseases, and no doubt the Empire Rheumatism Council will not be blind to the possibility.

The possibility of organizing periodic meetings on the lines of the American Rheumatism Association or the British Association of Physicians deserves to be explored and might lead to progress and to widening the interest in the subject. Such meetings, spread over one or two days and held perhaps every second year in different centres, aiming to attract general practitioners as well as specialists might, if well organized, soon become events of importance in the medical world.

AMERICAN RHEUMATISM ASSOCIATION

PROCEEDINGS OF THE REUNION MEETING

HOTEL COMMODORE, NEW YORK, MAY 24 AND 25, 1946

The meeting was opened by the President, W. Paul Holbrook, who said that this was the first occasion on which the American Rheumatism Association had met officially in joint session with the New York Rheumatism Association, who were hosts in what really was a special meeting. He paid tribute to the New York Rheumatism Association, which he believed was the only active rheumatism association to meet regularly during the war. He then welcomed distinguished guests from Canada and South America.

" Most of you remember ", he said, " that the American Rheumatism Association was conceived at the New Orleans meeting of the American Medical Association in 1932. Some of you were present at that first organizational meeting. You will remember the very learned but confusing discussions on primary arthritis, chronic infectious arthritis, arthritis deformans, rheumatoid arthritis, and so forth. Terminology and nomenclature were in a hopeless state of confusion, and none of us knew what the other fellow meant when he was talking about any of the various types of arthritis.

" Therapy was equally vague though enthusiastically prescribed. The use of chaulmoogra oil, specific vaccines, sulphur injections, mineral baths, bee venom, and a host of other therapeutic agents was seriously argued and discussed. This seems somewhat humorous to-day, but it wasn't then; it was a serious situation. Your Association is responsible in large measure for bringing order out of chaos so far as terminology and nomenclature are concerned. You are equally responsible for the many studies which have proved the worthlessness of the various therapeutic procedures then advocated. But this is not enough. Having arrived at a common language, and at a situation where we know there is no specific treatment for chronic rheumatic disease, we still have the major challenge ahead of us, and I should like to talk to you regarding four major goals.

" During the four war years this Association did not hold a meeting and took in no new members. Therefore, its first objective should be a wise and progressive enlargement of membership. In the armed forces alone there were over three hundred medical officers who worked on rheumatic disease projects. Most of these were young men who had developed a virgin enthusiasm and a sincere

interest in this problem. As far as possible these men have been invited by your Executive Committee to attend this meeting. It is your responsibility as a Society to maintain their interest in rheumatic diseases, and it is the obligation of those young men who are present to start at once to qualify for membership in this Association.

" Secondly, the work in public relations needs to be strengthened. I do not have to recall to you the March of Dimes for infantile paralysis, the Cancer Drive, the Tuberculosis Christmas Seals, and the Crippled Children's Program, all of which have been received enthusiastically by the public. There is as yet no such programme for the most important group of crippling diseases, chronic rheumatism. Such a programme must be devised, and must go forward under the direction and enthusiasm of this organization. I would suggest that the problem of research fellowships be seriously considered in this connexion. It is a concrete, simple request to the donor which he can understand, to provide funds for one research worker, or five or ten research workers, for fellowships in this disease. You will be glad to know that your Executive Committee has already taken favourable action on this recommendation, and I believe you may look forward to a strong programme in this respect.

" Thirdly, this Association in its early stages thought considerably of the general practitioner. While our right arm was engaged in research and in the advancement of knowledge about the disease, we have forgotten the obligations of our left arm, namely, to keep the general practitioners of this country constantly aware of the practical therapeutic problems in chronic rheumatic disease. Because we have no specific single aetiological factor, nor any specific cure, most of our physicians have either become therapeutic nihilists and have said, ' Nothing can be done for it ', or they have become one-shot artists, and have contented themselves with trying gold or vaccine or climate or transfusions or physiotherapy or some other single therapeutic aid. A really organized, adequate programme of therapy is seldom encountered throughout the country. In establishing a basic routine treatment I think you would agree that deformities should be prevented and anaemia corrected; that postural exercises are valuable; that diet and bowel management is important; that obvious foci of infection should be cautiously removed; that a balance between rest and activity should be prescribed; and that psychological adjustment of the patient to his disease is important. Yet these simple, basic things which are routine in the management of chronic disease—and there are more of them—are not yet known generally. Perhaps I should say this routine is known: it is in all the literature and there is nothing new about it, yet it has not been emphasized by our group to the doctors of the country. After the basic treatment some patients will then require gold, transfusions, fever therapy, change of climate, or vaccines, etc., all of which are of value provided the basic routine is first established. Such information should go to all physicians of this country, but especially to general practitioners, who are the first to see the patients.

" Fourthly, the New York Rheumatism Association has shown how affiliated societies in this country should be developed. I believe that you should go home to your community and, if possible, organize an affiliated rheumatism society. So far as I have been able to find, the New York Association is the only one that is affiliated with the American Rheumatism Association, though there are several other functioning rheumatism groups which should be so affiliated. This would offer us an outlet for public relations, scholarships, and money-raising, which could be done through local affiliated groups in various communities.

" In summary I should like to recommend that each of you add to the solution of our membership problem by finding suitable men and bringing them in as members. I urge that you enthusiastically support our programme of research and education, with research fellowships in rheumatic disease and the raising of funds even in a small way until the national programme can get under way. Most of you have at least one patient to whom you could sell the idea of contributing $2,500 or $5,000 a year for a two- or three-year fellowship. I have tried it on a few of my patients, and have found them interested in giving money for a concrete purpose. I recommend that we teach the physicians of this country what constitutes basic treatment, and that we emphasize how much can be done by such a programme, instead of how little! I also recommend that we organize an affiliated society in every community that can support one."

RHEUMATIC DISEASES AMONG AMERICAN SOLDIERS IN WORLD WAR II

PHILIP S. HENCH

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Dr. Philip S. Hench then read a paper on rheumatic diseases among American soldiers. He divided the rheumatic diseases, in their relationship to war, into two groups: (1) those peculiar to war and military service, and (2) those coincidental to war and military service. The first group comprised diseases of joints and related structures resulting from (*a*) infected wounds (septic joints), (*b*) excessive trauma of military type, as from long marches and accidents of paratroopers, (*c*) military herding, for example, epidemic rheumatic fever, articular complications of scarlet fever, meningococcal or streptococcal infections, (*d*) excessive exposure of military type to cold and wet, (*e*) excessive psychic trauma (" psychogenic rheumatism ") and (*f*) tropical diseases, for example, epidemic acute tropical polyarthritis (" fox-hole arthritis ", " Bougainville rheumatism ").

The second group, articular diseases coincident to military service, included: (*a*) recurrences or exacerbations of pre-existing rheumatic diseases, such as rheumatic fever, rheumatoid arthritis, fibrositis, gout, etc., (*b*) certain diseases which had their onset while the soldier was under no special stress, for example rheumatoid arthritis and osteo-arthritis, and (*c*) gonorrhoeal arthritis.

In an attempt to estimate what percentage of the rheumatic diseases which developed among soldiers was due to the war and what percentage was merely coincidental to the war, the expectancy for rheumatic diseases among a group of civilians the size of the Army had to be calculated. In how many of the men in uniform would " rheumatism " have developed aside from the hazards of war? According to the Hagerstom Survey (1921–1924), made by the United States Public Health Department, the annual incidence rate of rheumatic diseases was 19·6 per 1,000 citizens. At that rate, by considering the annual mean strength of the Army, about 353,000 cases of rheumatic disease would be expected to develop among soldiers between 1942 and 1944 ; actually about 332,000 cases of " rheumatism " developed among soldiers of the United States between 1942 and 1944 ; figures for 1945 are not yet available. In other words there developed in the Army just about the number of cases which could have been expected had the soldiers remained in civilian life. The incidence of rheumatic diseases among selectees for the recent Army was 9·0 per 1,000 as compared to 9·6 per 1,000 draftees for World War I; thus there seemed to be no more rheumatism among civilians of military age in this war than in the last. Despite this, some rheumatic condition developed in about twice as many soldiers in this war as in the last, since the rate of incidence of rheumatic diseases among soldiers in World War I was low, 8·16 per 1,000 soldiers.

Contrary to expectation the greatest incidence of rheumatic diseases as a whole was not among soldiers stationed in subarctic regions, nor was the lowest incidence among soldiers in the warm South Pacific theatres. There were more cases of rheumatic diseases as a whole in the Middle East theatre than elsewhere. The lowest incidence was in the Latin American theatre, but the incidence in the South-west Pacific was almost as great as that among soldiers in the North American theatre including Iceland. The incidence rate for rheumatoid arthritis did not follow geographically the incidence rates for rheumatic diseases as a whole. The greatest incidence of rheumatoid arthritis was not among soldiers in Alaska or Iceland, but among those in the South-west Pacific theatre, where there was twice as much rheumatoid arthritis as among soldiers in the United States, three times as much as among those in the North American theatre, and four times as much as in the Latin American theatre.

Hence climate, to the extent that it represents nearness to the equator, played an aetiologic role which was definitely secondary to that of other factors which operated locally around the soldier, or constitutionally, within the soldier. In individual cases, the favourable factor of serving in the warm tropics was more than offset by unfavourable local factors, such as long hours in a fox-hole or catching some prevailing infection provocative of some quiescent or larval form of rheumatic disease.

In contemplating the development of rheumatism in relation to the hazards of war it was surprising to discover that during both wars the incidence of rheumatic diseases among soldiers at home was definitely more than that among

soldiers in overseas theatres. Of course the best physical specimens were sent overseas.

Because of the large number of soldiers who had some rheumatic condition, the Army established five rheumatism centres, two for chronic rheumatic diseases and three for rheumatic fever. At the first centre, the Army and Navy General Hospital, about 7,700 rheumatic soldiers were admitted up to January, 1946. At the second centre, Ashburn General Hospital, about 5,500 rheumatic soldiers were admitted before the centre was closed in December, 1945. These two centres became the largest rheumatism centres in the world. The relative incidence for the various rheumatic diseases was about the same at these two centres, the chief diseases being rheumatoid arthritis and spondylitis, psychogenic rheumatism, osteo-arthritis, and fibrositis. But a great and most interesting variety of common and rare rheumatic conditions was encountered. The incidence of rheumatoid spondylitis was high. About 15 to 20% of all cases of " rheumatism " among soldiers sent to these two centres were cases of psychogenic rheumatism. Differentiation of psychogenic rheumatism from fibrositis, quiescent rheumatic fever, and mild rheumatoid arthritis was most important. Septic arthritis from combat wounds was handled so well in the forward echelons that it became a negligible factor. Gonorrhoeal arthritis was surprisingly rare, a triumph for chemoprophylaxis and chemotherapy. Of unusual interest were cases in which acute genital gonorrhoea precipitated, reactivated, or aggravated rheumatoid arthritis. It is not sufficiently understood, Dr. Hench said, that gonorrhoea could do this, and could act as a trigger mechanism for the development of rheumatoid arthritis just as certain other acute infections could do; namely, influenza, tonsillitis, scarlet fever, etc. At the rheumatism centre at the Army and Navy General Hospital more cases of " post-gonorrhoeal rheumatoid arthritis " were seen than cases of gonorrhoeal arthritis. Most of the former had been erroneously regarded as cases of gonorrhoeal arthritis resistant to sulphonamides or penicillin, or to both.

At the Army's five rheumatism centres various clinical studies were made, some of which have already been published; others will be forthcoming. As treatment centres and carefully supervised schools of rheumatology, these hospitals provided a unique opportunity which had benefited mutually both the rheumatic soldier and his medical officer. They afforded an unusual opportunity to give the rheumatic soldier the best available study and treatment and to advance knowledge of rheumatic diseases.

Discussion

Dr. Otto Steinbrocker (New York): Having completed a fifteen-year survey of civilian cases at Bellevue Hospital, a large metropolitan centre, I am interested in Dr. Hench's figures. It is revealing to compare his findings with our data in a large series. Do Dr. Hench's figures represent bedridden patients only, or ambulatory patients as well? One point that stands out from our findings and those of Dr. Hench is that tuberculous and gonorrhoeal arthritis and

possibly rheumatic fever, are statistically diminishing diseases. Our statistics showed a relatively small incidence of rheumatic fever in comparison with the other rheumatic diseases.

The problem of "psychogenic rheumatism", which Dr. Hench mentioned, is important. From our observations in the past five or six years I would say that Dr. Hench's figures are just about half of what we find in our arthritis clinic, and psychiatrists are apt to say that our statistics are too low. We find that at least 30% of cases sent us show major psychogenic manifestations. Of course Dr. Hench was dealing with a relatively young group. War of a fashion goes on all the time in everyday life. There are no explosions and there are no bullets in civil life but the effects of its psychogenic factors are cumulative. So the incidence of these disorders is likely to be higher in people in the older and middle-age groups than amongst younger people, even under the stress and strain of war.

DR. HOMER F. SWIFT (New York) : It would be unfortunate to group rheumatic fever under rheumatoid diseases and employ the symptom of arthritis as the sole criterion for the presence or absence of rheumatic fever, because other features of the disease may exist without polyarthritis as a presenting symptom. Dr. Steinbrocker has mentioned the decreasing incidence of rheumatic fever; and both statistically and clinically there is evidence that this is so. Twenty to thirty years ago it was common to find that during the late spring months from 30 to 50% of patients in the wards of our large metropolitan hospitals had the polyarthritic forms of rheumatic fever : to-day the proportion is much smaller. Nevertheless, there may not be a corresponding decrease in the incidence of rheumatic carditis; recent studies have shown the presence of carditis, with little or no polyarthritis, in many patients following group A haemolytic streptococcal infections. The only feature lacking to make a clear diagnosis of rheumatic fever was migratory polyarthritis; hence the question arises as to the probable necessity of revising our long-existing opinion that such arthritis is necessary for the diagnosis of rheumatic fever. My feeling is that it is not, and that many cases of chronic rheumatic valvular heart disease develop in patients who have had little or no arthritis. In this connexion the findings of Dr. Levy and his co-workers might be cited: in re-examining approximately 5,000 young adults who were rejected for armed service because of heart disease, it was found that approximately half had cardiac disabilities which were obviously rheumatic in origin; 69% of these men with rheumatic valvular disease gave no history of rheumatic polyarthritis or chorea; in Boston and Chicago the figures were approximately 85%. In evaluating Dr. Hench's data in so far as they apply to rheumatic fever in the Army, I think these non-arthritic cases should be kept in mind; while many valid indices show that rheumatic fever is decreasing in incidence, a false impression may be fixed in the minds of the public if we employ Dr. Hench's data to indicate the relative rates of such decreases.

DR. WALLACE GRAHAM (Toronto): Your president, Dr. Holbrook, was practically the father of our Canadian Centre. One foggy morning in London I boarded a 'plane to fly to Ireland. Seated next to me was an American medical officer. It was Dr. Holbrook. During the flight from London to Glasgow he gave me much information on the organization of the American Rheumatism Centre and suggested that I see Dr. Hench. The Canadian Government agreed, I spent five days with Dr. Hench, and so our Centre got under way. To date we have seen only 500 cases, but in the last review our percentage of fibrositis and osteo-arthritis was exactly the same as those noted by Dr. Hench; we noted a smaller percentage of rheumatoid arthritis and psychogenic rheumatism than he did.

DR. DARRELL C. CRAIN, Jr. (Washington, D.C.) : During the latter part of 1944, while I was with the Chief Surgeon's office in the South-west Pacific, I was amazed to note in a monthly report from the Surgeon General the high incidence of this disease being reported from our theatre. I checked with the orthopaedic consultant, who said, "Actually these cases are not of rheumatoid arthritis. Such a diagnosis simply affords a convenient way of getting a lot of the old crocks back to the United States. We don't have time to educate the medical officers in diagnosis, and these fellows are going home as cases of rheumatoid arthritis because they can be moved from the theatre that way easier than with other diagnoses. We don't have much true arthritis in this theatre."

DR. T. DUCKETT JONES (Boston): Does Dr. Hench think that the diagnostic criteria of World War I were sufficiently good for comparison with the diagnoses of this war? I think the diagnostic criteria have changed tremendously, in both rheumatic fever and rheumatoid arthritis, and I wonder if there has been any actual difference in incidence.

DR. DOUGLAS TAYLOR (Toronto): During the recent war I made a survey of rheumatic diseases in the Canadian Army Overseas, with interesting results. Among other things it was found that rheumatic disease constituted approximately 5% of all admissions to the Canadian hospitals before D-day.

In the breakdown of the figures on rheumatic disease into articular and extra-articular types there are some figures that require explaining. In various military hospitals I have worked in, and from figures published from other hospitals where a trained rheumatologist makes the diagnoses, the figures for articular diseases run from 30 to 36% only, whereas the other 70 to 64% of cases are extra-articular conditions, including fibrositis. In civil medicine, in arthritis clinics, the proportion seems to be reversed, i.e. articular diseases are approximately 75%, and extra-articular conditions 25% (with numerous individual variations). However it is to be noted that, of the rheumatic diseases in the American Army for World War I, 85% were articular and 15% non-articular. Also in the Canadian Army Overseas as a whole, in World War II, the figure reported for articular diseases was 84·7%. In other words, in the Army, composed of presumably healthy young men, the proportion of articular to non-articular rheumatic conditions seems to approximate 85 : 15, roughly the same as that found in civilian clinics where the patients are men and women of all ages! That seems difficult to believe. Apparently many patients in the Army with symptoms of rheumatic disease are diagnosed as having " arthritis " whereas the condition really is some type of extra-articular condition. Probably the reason for this is the lack of diagnostic criteria for the various types of arthritis. Medical officers presumably are not sufficiently trained in rheumatic diseases, so that the term " arthritis " is used too freely in diagnoses; and medical officers are the practitioners in peace-time. It is suggested, therefore, that to Dr. Holbrook's four desiderata we add the establishment of diagnostic criteria for distinguishing the various types of rheumatic diseases. Patients with extra-articular conditions should not be diagnosed as suffering from " arthritis ".

DR. RUSSELL L. CECIL (New York): I am sorry Dr. Hench did not have more time to define clearly what he included under the heading of psychogenic rheumatism. Of course we see a great deal of it in civilian life, for example occipital pain and pain in the neck—the occipital headache which Dr. Harold Wolf has described. The patient with this pain in the neck has an amazing capacity to reproduce a similar syndrome in the examining physician! I wonder if it should be classified as psychogenic rheumatism or as fibrositis. Some of it is due, of course, to osteo-arthritis of the spine, but in these young soldiers that could be eliminated.

DR. PHILIP S. HENCH (closing): I beg to differ with Dr. Steinbrocker's opinion that the incidence of psychogenic rheumatism is higher among civilian than among military patients. The figures given for the relative incidence of psychogenic rheumatism at the Rheumatism Centre, Army and Navy General Hospital, represent only those cases in which psychogenic rheumatism was the only or the major or dominant problem. In a military hospital almost every rheumatic patient sooner or later presents some functional overlay. The relative incidence of psychogenic rheumatism would have been much higher had we also included here patients who had rheumatoid arthritis or some other organic rheumatic disease and who had also a definite but minor functional overlay. In my opinion there is more psychogenic rheumatism, and it is generally more severe, among soldiers than among civilians. However, many civilians do suffer from varying amounts of psychogenic rheumatism, and it certainly behoves civilian practitioners to recognize it and not to treat it as, for example, " fibrositis ".

Dr. Swift is correct when he states that my figures for rheumatic fever among soldiers may be inaccurate if they do not include cases in which rheumatic fever was manifested only by rheumatic heart disease and not by rheumatic polyarthritis. The figures that I have presented,

which I obtained from the Office of the Surgeon General, represent cases in which the diagnosis was " acute rheumatic fever " or " rheumatic fever ". Undoubtedly most of these cases were of acute rheumatic polyarthritis. I hope to add later the figures for rheumatic heart disease without " acute rheumatic fever " or rheumatic polyarthritis.

Dr. Crain challenges the accuracy of the Surgeon General's figures for rheumatoid arthritis in the South Pacific, stating his belief that in that theatre of operations the diagnosis of rheumatoid arthritis was unfortunately too often used as a diagnosis of convenience, a mechanism whereby a misfit or a homesick soldier who had minor musculo-skeletal symptoms was invalided home. If this is true, it would be unfortunate indeed and a reflection on the professional integrity of his medical colleagues in that region. Neither the Surgeon General, nor I, nor anyone else could correct these figures without a case-by-case review. I have given the figures made available to me by the Office of the Surgeon General, which accepted them in good faith. However, I shall discuss with them Dr. Crain's contention and see what can be done to check it.

As to the accuracy of the various diagnoses, most of the figures I have given are no more accurate than the diagnostic level of the medical profession as a whole, and we of the American Rheumatism Association know what that is in matters rheumatologic. However, the figures presented from the Army's rheumatism centres were obtained only after group consultation by medical officers especially trained in rheumatology: they are the figures from World War II which the Office of the Surgeon General has compiled, and which, with minor corrections, will undoubtedly be quoted from now on. If the American Rheumatism Association would like to support one or more research fellows to review individually the Army's cases, or a substantial sample thereof, perhaps a useful factor of correction might be obtained. But I suspect that we shall have to accept these figures " as is " and for what they are worth.

Dr. Jones has suggested that the medical profession of this generation is probably so much more accurate in diagnosing rheumatic diseases than were medical officers during World War I that it is futile to compare the figures for the two wars. Certainly, rheumatologists and internists interested in rheumatic diseases are more accurate than their predecessors were twenty-five years ago, but I am not so sure that the average modern practitioners are much more accurate in diagnosis of rheumatic diseases than they were in World War I. The practitioners of to-day are still calling many cases merely " arthritis " or " chronic arthritis ", and what that may mean heaven only knows ! Considering the incidence of the inclusive term " rheumatism ", the incidence of rheumatism among selectees was 9 per 1,000 in World War I and 9·6 per 1,000 in World War II, suggesting that civilians of military age twenty-five years ago had about as much rheumatism as now. But taking my figures as a whole there were more than twice as many *soldiers* (per 1,000) who developed some rheumatic disease during World War II as during World War I. Dr. Taylor suggested that all or many of these cases should be grouped together and labelled " fibrositis ". Frankly, such an attitude disturbs me. Some of us have tried hard to clarify the term " fibrositis " and make it represent a characteristic symptom-complex, a clinical entity. " Fibrositis " to us does not represent just aches or pains anywhere of any type. Fibrositis produces symptoms of a characteristic type and location and with a characteristically good prognosis as far as articular structures are concerned. Those who use the term glibly, carelessly, or all-inclusively to cover any vague musculo-skeletal symptoms do rheumatology a disservice.

I am uneasy about recent British figures on the incidence of fibrositis among civilians or soldiers. It has been stated that about 70% of the rheumatic soldiers in British military hospitals had fibrositis. No figures on the relative incidence of psychogenic rheumatism were given. Is the differentiation between fibrositis and psychogenic rheumatism adequately considered by British medical officers and rheumatologists? Are most of their cases of psychogenic rheumatism included under the term " fibrositis "? If so, it is such inaccuracy of diagnosis which makes it difficult for those of us in this country to bring an understanding of, and dignity to, the concept of fibrositis, an entity originally defined by British physicians.

ADULT RHEUMATIC FEVER

EPHRAIM P. ENGLEMAN
San Francisco

Dr. Engleman described a study based on 478 consecutive admissions into an Army Service Forces rheumatic fever centre from one to six months after the onset of the disease. Total hospitalization lasted from six to twenty-four months. Most patients had had no previous attack, but the incidence of a family history of rheumatic fever or arthritis was significantly high. Arthritis, the commonest and usually the earliest indication of rheumatic activity, was progressive more often than migratory. Although there were no objective residual joint symptoms, pains in the joints frequently persisted as long as thirteen months after all signs of active disease had disappeared, Seventy-eight per cent. of the patients showed evidence of carditis. Abnormality of the electrocardiogram occurred in nearly 50%, thereby emphasizing its diagnostic importance. The commonest abnormalities were heart blocks and T-wave changes; the latter were confined in nearly 10% of the pathologic tracings to the precordial lead. Additional signs of rheumatic activity, in order of frequency, included elevation of the sedimentation rate, fever, leucocytosis, purpura, erythema, pleuritis or pneumonitis, nodules, and chorea; 64% showed normal monthly anti-streptolysin titres. Rest in bed was a valuable therapeutic adjunct despite certain limitations. Salicylates during active disease apparently protected against recrudescence of arthritis. Compared with the disease in children, adult rheumatic fever was a relatively benign disease with a comparatively good immediate prognosis. Follow-up studies were urged by Dr. Engleman.

Discussion

Dr. T. Duckett Jones (Boston, Massachusetts): The seemingly low incidence of permanent heart disease is much in keeping with our civilian experience concerning patients who develop rheumatic fever in adult life, the majority of whom have escaped any serious degree of heart disease up to the present time and who, judging from experience, will escape it permanently. One reason why the incidence of cardiac disease is so low may be because Dr. Engleman was dealing with males rather than females. There is a very different pattern in rheumatic fever in adult life between the two sexes. Why that should be true I do not know. One practically never encounters insidiously developed mitral stenosis with a reasonably normal-sized heart in the adult male. It is quite common in women. I presume that the majority of these men will not have mitral stenosis—or any other real evidence of heart disease—several years from the illness contracted in the services, unless they develop recurrent rheumatic fever. The incidence of rheumatic fever in the general population in the age group of these men is relatively low. I do not know why, but I presume it is because we do not have a tremendous amount of exposure at that age to the infections that are common in children. Women have rheumatic fever more often than men.

I am at a loss to understand why 64% of Dr. Engleman's patients should have had normal anti-streptolysin titres. In a rather extensive study of rheumatic fever in the Navy, anti-streptolysin responses were observed which indicated recent streptococcal infection in nearly 100% of patients. I wonder how soon after rheumatic fever started the titres in Dr. Engleman's cases were determined. Also, I would like to know what part of the country this study was done in, and where the rheumatic fever occurred.

Were the patients with normal sedimentation rates on salicylates? It has been our experience that once rheumatic fever patients get over the acute or initial symptoms the sedimentation rate can be brought to normal by adequate doses of salicylates. You can keep salicylates up for months, and still have many sedimentation rates become abnormal within two weeks after the withdrawal of the drug. Were the symptoms after withdrawal of salicylates considered to be a recurrence of the disease? I think such symptoms merely represent a withdrawal pattern. Patients who have had rheumatic fever for a long time often get some rise in temperature and even some symptoms upon withdrawal of salicylates.

DR. JOHN G. KUHNS (Boston, Massachusetts): Dr. Engleman mentioned that in many cases there was a deflection of the T-wave in T-2, T-3, and especially T-4. Does not a deflection of the T-wave indicate pericarditis, and is it not preceded by clinical symptoms in the patient? The usual rheumatic deflection we see is a prolonged interval and not a deflection of the T-wave unless there is a pericarditis.

DR. HOMER F. SWIFT (New York): How many specimens from each patient were examined for determining the anti-streptolysin titre? Our own figures from an age group very similar to his were much higher; approximately 90% of our patients showed significant increase in this antibody. I have noticed in many reports during the war period that the figure for anti-streptolysin abnormalities were based on one or two determinations. The anti-streptolysin curve follows just as many variations as any other feature of streptococcal infection. There may be a delay in a rising titre, or it may be early. I think that your figures concerning this antibody are out of tune with the experience of many observers who have made more frequent tests. Possibly the period in the disease when the blood was taken from the patients may have been a factor in these discrepancies.

DR. E. P. ENGLEMAN (closing): We were aware of the fact that our anti-streptolysin figures were " off key " as far as the literature is concerned. These titres were done under the supervision of Dr. Lowell Rantz, who was the civilian consultant in rheumatic fever for the Ninth Service Command; and his experience with other patients in this same age group has been similar to ours. Anti-streptolysin titres were done once monthly, starting as soon as the patient was admitted. It is possible that the reason our titres were unusually low was because in many instances our patients were not admitted into the centre until six to twelve weeks after the onset of the disease, although it is my impression this should not have made much difference. The titres were done once monthly, and these patients were hospitalized in the centre for anywhere from three to sixteen months, so that in most cases we had a minimum of two or three monthly titres, and in many cases more. I have no explanation for the results of our titre determinations. Perhaps the age group was an important factor.

We did not see severe toxic reactions to salicylates. These patients were seen in a rheumatic fever centre to which patients were usually brought after the acute manifestations of the disease had subsided, so that it was not necessary to use salicylates as often as it might have been had we seen the patients earlier. Salicylates were usually discontinued when the sedimentation rate became normal. The patient was then made to rest in bed for another week or two. In most cases we were not able to demonstrate any remarkable relationship between the administration of salicylates and the sedimentation rate. If salicylates were discontinued in the presence of an elevated sedimentation rate, and perhaps nothing more, it was not unusual to see an acute exacerbation of the arthritis.

I am aware that pericarditis is thought to be a possible cause of T-wave changes. In most of these cases, however, there was no reason to suspect pericarditis; usually no friction rub was described; there was no remarkable precordial pain, and no effusion. Pericarditis was not clinically demonstrable in most cases. Nevertheless we wish to emphasize that we did see significant changes in T-1, T-2, and T-4 in a large proportion of the cases.

Routine prophylactic sulphonamide therapy was not used. Incidentally this study was performed in sunny Southern California and in beautiful Palm Springs, and it would have been contrary to the policy of the Chamber of Commerce even to suggest the use of sulphonamide prophylaxis. (Laughter.)

EPIDEMIC TROPICAL ARTHRITIS

DARRELL C. CRAIN

Washington, D.C.

The purpose of this paper is to call to the attention of American physicians interested in rheumatic diseases an acute syndrome observed in epidemic proportions among American and Australian troops in the Northern Territory of Australia and characterized by polyarthritis, an exanthema, generalized lymphadenopathy, and fever. The disease was described in the Australian literature by Halliday and Horan,[1] while a report of the syndrome was submitted to the Chief Surgeon of the United States Army in the Far East by Hidde.[2] A similar epidemic occurring in Australian troops stationed in Northern Queensland has been reported by Sibree.[3] All these papers referred to the syndrome as " polyarthritis "; a more descriptive term would seem to be " epidemic exanthematous arthritis "; however, as this term may cause confusion with Haverhill fever, the name " epidemic tropical arthritis " has been used in this paper.

Occurrence.—The disease was first noted in September, 1942, among troops of both the Australian and American Armies stationed in the Northern Territory of Australia in and around Darwin. It then progressed southward, spreading in epidemic form, with cases being reported as far south as Mount Isa, some eight hundred miles distant. This area, geographically, is tropical and the period of the year was that during which the weather was hot and dry. With the onset of rains in January the epidemic ceased abruptly, to recur in the same area during the corresponding period the following year.

Clinical Course.—The onset of the disease was gradual, with the customary prodromes of acute infections noted for twenty-four to forty-eight hours: anorexia, headache, lassitude, etc. These, however, were at times absent or recalled only in retrospect upon questioning, with the first symptom noted being

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[1] *Med. J. Austral.*, 1943, **2**, 293.
[2] Unpublished report to the Chief Surgeon, U.S. Army, Far East, Jan. 29, 1943; on unusual cases of polyarthritis.
[3] *Med. J. Austral.*, 1944, **2**, 565.

either a maculo-papular rash, or swollen, painful joints, either being followed by the other in twenty-four to forty-eight hours. Generalized lymphadenopathy and fever were found upon examination. The disease usually pursued a mild or moderate course lasting seven to fourteen days with complete recovery. Some cases were so mild as to permit continuation of a " light duty " status with complete recovery in five days; a few were of marked severity lasting three to five weeks; and a very occasional recurrence after six to twelve weeks was observed. No residual cardiac or joint damage was noted.

Signs and Symptoms.—A detailed description of the significant signs and symptoms will serve to identify the distinguishing characteristics of the syndrome.

Joint manifestations.—Some form of joint involvement was present in all cases and constituted the most distinctive single feature of the disease. Although the small joints of the hands or fingers were most commonly affected, no extremity joint was immune; involvement of the spine, however, was rare. Multiple joint involvement was the rule, and this was at times migratory. Pain, stiffness, and limitation of motion were the symptoms complained of, while examination revealed swelling and tenderness of a mild to moderate degree. While periarticular thickening was most common, a true effusion with local heat was often found. Fusiform swelling of the fingers as is seen in true rheumatoid arthritis was a frequent finding. Concurrent involvement of supportive structures such as fascial planes, tendons, or bursae was also noted. Although stiffness and some limitation of motion often persisted for some time after the disappearance of other signs and symptoms, residual joint damage or muscular atrophy did not occur.

Rash.—Although not present in all cases, a more or less typical exanthema was sufficiently common to be considered a distinctive feature of the disease. This was of a maculo-papular or even a vesicular nature, resembling the rash seen in chicken-pox. Unlike this latter disease, however, all lesions appeared simultaneously rather than in " crops ". The rash occurred most commonly over the upper portion of the trunk and the extremities; the face and mucous membranes of the palate were involved only in the most severe cases. The appearance of the rash either preceded or followed the first joint symptoms but in either case usually disappeared before the latter subsided. In many cases the severity and extent of the exanthema was not related to the severity of other symptoms, a very light rash or none at all often accompanying severe constitutional and joint symptoms, and a very deep extensive rash being noted with minimal joint symptoms. The height of the exanthema was reached in twenty-four to seventy-two hours, and fading without desquamation or rupture of vesicles occurred in from two to ten days.

Lymphadenopathy.—Generalized, moderate enlargement of lymph glands was a constant feature, but splenomegaly was not noted. Although the extent and degree of the lymphadenopathy varied, involvement of all superficial glands, even the epitrochlears was observed. The glands were discrete, usually soft or rubbery, and often painful as well as tender. When present, these latter symptoms usually

disappeared in two or three days, although symptomless enlargement sometimes persisted for days or even weeks after all other symptoms had subsided.

Fever.—Fever consistent with the severity of constitutional symptoms and joint involvement was present in all cases. Since most cases tended to be mild the temperature was often below 100° F. and tended to return to normal in two to three days. However, fever occasionally rose to 104° F. with severe prostration, while a recurrence after two to three days' normal temperature indicated exacerbation of joint symptoms.

Miscellaneous.—Malaise ran parallel to the fever and joint involvement and was accompanied to a varying degree by anorexia, headache, and photophobia. A curious symptom sometimes noted was a transitory hypersensitivity of the finger-tips. Constitutional symptoms were at times entirely lacking in the milder cases.

Laboratory Findings.—Blood counts, urinalyses, and agglutinations showed no significant abnormalities other than a mild leucocytosis to nine or ten thousand, with a normal differential count. Halliday and Horan reported increased sedimentation rate during the " active phase " of the disease, returning to normal as symptoms subsided. They also reported negative blood, stool, and urine cultures, and found that cultures from the tonsils and nasopharynx showed no significant abnormalities.

Differential Diagnosis.—Dengue, acute rheumatic fever, early rheumatoid arthritis, palindromic rheumatism, Haverhill fever, and acute exanthemata presented the chief sources of confusion in diagnosis. The disease often resembled dengue so closely that accurate differentiation was not possible where both conditions were occurring simultaneously in epidemic form. In clear-cut cases, however, the rash of epidemic tropical arthritis was more apt to present a discrete, raised, papular, or vesicular appearance as contrasted with the macular rash of dengue. Furthermore, constitutional symptoms were usually less severe than in dengue where the " break-bone " syndrome is liable to involve the muscles and bone rather than the joints. Lymphadenopathy is rare in dengue, and leucopenia is the rule; both these situations were reversed in epidemic tropical arthritis.

The disease was differentiated from early rheumatoid arthritis by the rash, lymphadenopathy, and rapid clearing without residual joint involvement, from palindromic rheumatism by the absence of previous history of involvement and by the epidemic nature of the disease, and from Haverhill fever by the more gradual onset, the generally milder course of the disease, the existence of rash on the face and trunk, the predilection for involvement of the small joints of the fingers and hands, and the absence of intermittent or remittent fever. Isolated cases with minimal joint involvement were at times confused with either measles or chicken-pox, but the appearance of the typical joint symptoms usually established the diagnosis.

Treatment.—As no specific therapy was known, treatment was purely symptomatic. Although salicylates relieved the joint pains, they had no apparent effect

on the course of the disease. Immobilization of the affected joints was not considered necessary.

Aetiology and Transmission.—All factors pointed toward the disease being an acute infection, but attempts to isolate the specific aetiology were fruitless. Halliday and Horan reported negative results with blood from two cases and aspirated joint fluid also from two cases when inoculated into rats, guinea-pigs, mice, developing hen's eggs, and a single monkey. In the epidemic of both years the appearance of the disease corresponded with the beginning of the summer season, when there was an increase in the mosquito population. However, this was probably purely coincidental, as the epidemic ended abruptly as the rains began and it is during this latter period that the mosquito population is greatest. The author knows of no case which was preceded by a rat bite.

Summary.—Clinical features of a syndrome occurring in epidemic form among American and Australian troops stationed in the Northern Territory of Australia and characterized by polyarthritis, fever, lymphadenopathy, and erythema have been described. The disease was probably an acute infection although no specific aetiological agent was identified. All cases made a complete recovery, and residuals were not noted.

Discussion

Dr. Philip S. Hench (Rochester, Minnesota) : At the Army and Navy General Hospital certain of our patients who had returned from the South Pacific spoke of this disease as " fox-hole arthritis " or " Bougainville rheumatism ". About 400 cases have been summarized in the seven (four American and three Australian) reports on this disease. The first of these reports was prepared by Captain Frederick G. Hidde of the American Army and was dated January 29, 1943; considered a " secret document ", it was not published. This, and a later report by Lieut.-Col. Bert E. Mulvey and Captain Francis McCarry, were excellent, and illustrate what fine work interested medical officers can do when they encounter a new disease even under the unfavourable conditions of field service. These medical officers met the problem of the new rheumatic disease in a way that deserves the whole-hearted approval of this Association. It is unfortunate that the four reports of the American medical officers were considered secret documents and have not yet been published. In contrast the Australian medical officers were able to publish their excellent reports promptly.

If my review of these reports is correct, it appears to me that the disease among the Australians in the Northern Territory reached its peak of incidence each year in October or November and faded away in December. However, when the disease affected American troops in New Guinea and Bougainville, it began each year about two months later, yet the climate in these places is not, equatorially speaking, two months behind that of Northern Australia. Does Dr. Crain have any explanation for this difference in the time of appearance of the disease?

Dr. Douglas Taylor (Toronto): It would be interesting to know whether or not radiological studies were made in these patients, to determine intra-articular involvement. Fluid was obtained from some of these joints; but that could occur in a simple synovitis or in conditions like rheumatic fever. In many tropical diseases synovitis or " arthritis " is given as one of the complications. Consequently one wonders if instead of a " new type of arthritis " these cases may not be some type of tropical disease with a temporary polysynovitis as one of the findings (along with the rash, fever, and adenitis).

Dr. Walter Bauer (Boston, Massachusetts): Did the available bacteriological facilities

allow repeated attempts to isolate *Strep. moniliformis*? Unless such studies were made it is impossible to rule out a mild form of Haverhill fever.

DR. SAENZ (Peru) described a type of arthritis, gastro-intestinal and probably allergic, which was epidemic in Peru and appeared to be identical with that which Dr. Crain had described in Australia.

DR. DARRELL C. CRAIN (closing): Dr. Hench has brought up what may be a significant point; the epidemics in the Northern Territory occurred just before the heavy rains, during a particular season of the year; then in Bougainville and also in Oro Bay they again occurred at specific periods only. It seems quite possible that there was a relation between the season and the epidemics—possibly an insect vector which was only present at a certain time of the year.

In the third year that the troops were in the Northern Territory Col. Maurice Pincoffs, Chief Medical Consultant at the time, was interested and we were going to fly a group up to Darwin to do some investigative work, and then no epidemic occurred. Col. Pincoffs thought it might be related to coccidioidomycosis, although neither of us had ever seen a case of coccidioidomycosis with joint involvement.

I must admit to the paucity of expert laboratory work. The Australians had a much larger garrison than we had, including a large general hospital; ours were only small station hospitals. Almost all the laboratory work was done by the Australians, but even so it was quite inadequate. Our facilities were very poor; when the symptoms were of acute polyarthritis with fever, we naturally suspected rheumatic fever, and yet we could not even get cardiograms done.

Dr. Taylor asked whether this might be simply another tropical disease. He is quite right to ask; and I have indicated as much in the name I am using for the syndrome. The reason I have called it arthritis is that I do not agree with him that in all true arthritis you have radiological evidence of changes. These people had true arthritis: effusions in the joint which were sufficient to be tapped, and fusiform swelling of the hand similar to that in rheumatoid arthritis. So this may be entirely a tropical disease.

As to the point Dr. Saenz brought up, our cases did not appear to be allergic; the syndrome looked much more like an epidemic as it spread among the troops. It could well have been spread by alimentary means as we had many diarrhoeas all over this area.

PAINFUL HOMOLATERAL DISABILITY OF SHOULDER AND HAND WITH SWELLING AND ATROPHY OF HAND

OTTO STEINBROCKER
New York

Dr. Steinbrocker had observed and treated six cases with certain distinctive clinical features which had occurred in the past nine years amongst over two hundred patients with painful disability of the shoulder. There was no history of antecedent trauma or coronary disease. These cases were distinctive because of the characteristics indicated in the title and other features to be discussed. The aetiology was not clear. Dr. Steinbrocker had examined whether the clinical

picture represented merely a complicated form of fibrositis in the shoulder and neck, some vascular or neurological disturbance, especially a sympathetic neuropathy, or a special syndrome showing certain distinctive signs. He said that the shoulder-hand disorder deserved to be emphasized because almost every case had during its various stages been diagnosed as rheumatoid arthritis, periarthritis, scleroderma, scalenus anticus syndrome, post-infarction sclerodactylia, or some other condition. Some of the patients received gold salts, radiation therapy, and other treatment at least of doubtful value. As a purely diagnostic problem embracing a combination of symptoms apt to be misdiagnosed, this shoulder-hand syndrome was worthy of emphasis. Dr. Steinbrocker had used regional spinal nerve and sympathetic block on these patients. One of them was referred for surgical exploration of the neck and section of the dorsal sympathetic nerves. In two of them venograms were done with suggestive results. Dr. Steinbrocker said that the present discussion was intended to crystallize the clinical picture so that it might be differentiated from similar conditions, notably " post-infarction sclerodactylia." In this idiopathic group with shoulder-hand symptoms the gravity of the prognosis in some cases was shown by disability and contractures of fingers lasting from two to nine years, in one case probably permanent.

Discussion

Dr. R. M. Stecher (Cleveland, Ohio): In two patients similar to those described by Dr. Steinbrocker the difficulty began after manipulation of the shoulder. One had a so-called " frozen shoulder " which had been treated in an airplane splint for several months. When the splint was removed the shoulder was stiff in an abducted position. The surgeon in charge decided to free the shoulder and he brought the arm down forcibly. From that time on the patient had considerable pain and complete disability in her right arm. She was referred to me as a possible case of gonorrhoeal arthritis, because the hand and wrist were very painful, swollen, and cyanotic. Radiographs revealed an unrecognized fracture of the shoulder. There was marked atrophy of all the bones of the upper extremity and a lead-pipe stiffness of the joints.

The other patient was similar in that she had a stiffened shoulder which had been manipulated. Afterwards she had the symptoms of a mild ulnar and median nerve palsy. This patient had a poorly developed hand because of poliomyelitis in early childhood, and there was consequently marked atrophy of all the muscles of the extremity. Both patients recovered satisfactorily with vigorous physiotherapy. The bone atrophy in the second patient has remained because it was due to lack of development. This particular patient is being described elsewhere because she developed Heberden's nodes on her sound hand but did not develop them on the atrophied hand.

The radiographs in this condition are not typical of rheumatoid arthritis. There is marked bone demineralization which, however, is spotty. The joint spaces are normal, the joint surfaces are regular and smooth, so there is no evidence of erosion or distortion of the joint surfaces themselves. We have always called this Sudeck's bone atrophy, a condition which is supposed to be due to some neurotrophic disorder, the nature of which is not recognized. It is presumed that bone atrophy under these circumstances results from increased circulation of the blood to the bone. Some patients have recovered with vigorous physiotherapy, but periarticular stripping and other similar nerve operations have been recommended.

Dr. H. G. Kupperman (New York): I have treated a painful frozen shoulder or periarthritis, associated with a Dupuytren's contraction of the hand, which was restored to normal by means of brachial plexus nerve blocks and manipulation of the shoulder joint. I venture to say it is

possible that a chronic frozen shoulder can produce, due to disuse of the extremity, atrophy and osteoporosis of the hand, or due to sympathetic involvement, a condition similar to Sudeck's atrophy. De Takats * believes that these cases of osteoporosis, whether due to Sudeck's atrophy or post-traumatic osteoporosis, are sympathetic in origin and in that respect similar to the causalgias. The syndrome described here might be placed in the same category, and I suggest that in the early stages sympathetic blocks combined with brachial plexus nerve blocks and manipulation of the shoulder joint might possibly be useful in preventing chronic disability.

Dr. Roland Davison (San Francisco): How does this syndrome differ from that described by Oppenheimer, which is due to radiculitis from cervical arthritis? I have seen many of these patients, ten in our clinic at San Francisco in the past year. The radiographs should be studied carefully, particularly semi-lateral views, in which the patient should be fluoroscoped so as to be sure to demonstrate the foramina well. The symptoms in the hands are undoubtedly due to radiculitis.

Dr. William J. Kerr (San Francisco): This condition is not uncommon in association with coronary disease, especially with coronary occlusion, and I believe the reason is relatively clear. For many years past it has been the common practice of clinicians to confine to bed those patients who have had an attack of coronary occlusion, and to keep them absolutely quiet for a relatively long period. It has been my experience that a very high percentage of these patients develop a " frozen " or stiff shoulder. Almost all of them will develop shortening of the pectoralis and latissimus muscles and tendons, and the picture is not unlike that seen in scleroderma. It does bring the problem close to what Dr. Steinbrocker and others have mentioned about causalgia and other types of injury, and to peripheral lesions of bones and tissues where apparently the reflex arc is attacked at another point.

We have heard a good deal recently about the effect of using procain or other material to interrupt the sympathetic pathways. Evidently it does some good in some cases, not in all. Apparently the synapses, as has been pointed out recently, are made more sensitive, so that this whole reflex arc may be affected, with abnormal responses in the sympathetic or the vasomotor fibres. We have probably all seen patients with rheumatoid arthritis who had symptoms like Raynaud's disease, with a peripheral neuritis present for a considerable time before there was demonstrable involvement of the joints.

Dr. Richard H. Freyberg (New York): This is a condition that we have recognized both at Ann Arbor and in New York. We have called it the " shoulder-hand syndrome ", because it is not understood and this name merely indicates the parts that are involved. The elbow has never been involved. It is not rheumatoid arthritis, and there are all degrees of severity. The disability following it is relative to the severity and duration of the illness. It deserves more study.

Dr. Edward F. Rosenberg (Hot Springs, Arkansas): A good deal of information about this condition may be found scattered in the literature under a variety of titles, including peri-arthritis, Sudeck's atrophy, Oppenheimer's hand, sclerodactylia, causalgia, painful bone atrophy, post-infarction sclerodactylia, and others. We have recently made biopsies of the wrist in two such cases. In one we found tuberculosis. In the other the synovia was normal in appearance. We have studied the condition of the heart carefully: in the majority we found the heart normal. On the other hand, we have seen the same condition following coronary occlusion. It appears that this type of swelling and pain in the hand is a non-specific reaction to a variety of causes, including periarthritis of the shoulder, prolonged immobilization, local trauma, hysteria, heart disease, and local infections. Doubtless the same reaction may be produced also by other causes. Did Dr. Steinbrocker perform any biopsies?

Dr. Philip R. Trommer (Philadelphia): A possible neurophysiological explanation for this mechanism may be as follows. The existence of muscle spasm in poliomyelitis as a major cause

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* *J. Amer. med. Ass.*, 1945, **128**, 699.

of deformity has been clinically shown by Elizabeth Kenny. This muscle spasm may be due to involvement of the internuncial cells, which are located around the central canal of the spinal cord between the anterior and posterior horns. These cells are the end points or " switchboard " through which almost all impulses reach the anterior horn cells. Involvement of these cells results in muscle spasm—simulating an upper motor neuron lesion. This has been postulated by Dr. Kabat as the lesion in poliomyelitis producing muscle spasm. In the lateral portion of the anterior cell horn sympathetic synapses are located in close proximity to anterior horn cells. Russian investigators believe the internuncial cells exist on a higher level than the anterior horn cells or sympathetic synapses. There is evidently a good deal of ipsi- and contralateral overlapping in the cord among these cells, and this explains involvement of opposite limbs. Evans, of the Lahey Clinic, believes that the cumulative effect of prolonged bombardment of the internuncial cell pool by pain impulses constantly activates the involved synapses, and calls this syndrome " reflex sympathetic dystrophy " when it also involves the circulatory system. Although the *modus operandi* is not entirely clear, it is possible that in this manner symptoms and signs of muscle spasm and cramps are produced (internuncial cell involvement); cyanosis, oedema, and blanching of the skin (sympathetic cell involvement). Prolonged vasoconstriction may thus produce osteoporosis and the so-called Sudeck's atrophy, which may be the same process.

DR. PHILIP LEWIN (Chicago): There is an interesting phenomenon that occurs in many of these patients. Those who have much pain will tell you that the only relief they have ever obtained is in swinging the hand in a pendulum movement.

I would like to hear Dr. Steinbrocker say more about treatment. So far, all the improvement seems to have been automatic.

DR. PICKARD (Kansas City): In cases developing after manipulation of the shoulder some consideration should be given to the possibility of true brachial plexus injury occurring in consequence of the manipulation. I have had such an experience in a case in whom there was marked condensation of the bone in the glenoid, with approximation of the head of the humerus to the scapula.

DR. OTTO STEINBROCKER (closing): This syndrome is not quite Sudeck's atrophy, in our opinion. None of the cases, with one doubtful exception, had a history of local trauma or infection of any kind, and as far as I can tell from the literature on Sudeck's atrophy there usually is such a history. We have had a few cases of disabling dystrophy resembling this condition in many ways, but in each of them there was a story of trauma. One patient who presented a clinical picture in many respects similar to what I have shown, suffered from a digital osteomyelitis which was operated, and shortly thereafter she began to develop post-traumatic dystrophy. We do not know enough about this syndrome, so for the present in every case it is safest to exclude a myocardial infarction. That is the most serious threat to the patient. The other possible aetiologic factors are less serious. No patient with this syndrome, therefore, has been completely studied unless an electrocardiogram has been done.

The shoulder-hand syndrome and so-called " post-infarction sclerodactylia " may well represent aspects of a very large group of disorders with a number of subgroups activated through the disturbed sympathetic nerve supply. Undoubtedly there must be many aetiologic factors producing a more or less similar clinical picture, arising when the same mechanism is brought into play, and giving a stiff shoulder with a swollen and trophic hand. By discussing the fundamental question of the sympathetic role here, and treatment on that basis, it will probably answer several of the questions that have been raised. We were impressed with the possibility of the sympathetic nerve supply playing an important part in the production of this picture as in similar conditions and, for that reason, we used procain injections. We have employed three approaches so far. First, we gave these patients brachial plexus blocks. I cannot draw any therapeutic conclusions from six patients, but as far as we have gone we have been very much impressed in three of the cases by the rapidity with which they obtained a return of shoulder function and relief of shoulder pain. The brachial plexus block has no effect upon the evolution of the hand

symptoms, but it does seem to accelerate the return of shoulder function and shoulder comfort. Alf Johnson described post-infarction sclerodactylia and gave some clear ideas of the mechanism which may explain it. He suggests that the shoulder disability may originate differently from the hand symptoms. This supposition may be correct, because the shoulder responds to brachial plexus injection while the hand involvement does not.

Secondly, we carried out repeated sympathetic injections and got excellent blocks of the stellate ganglion, evidenced by a Horner's syndrome and flushing of the extremity—satisfactory blocks from a technical standpoint, but the two patients so treated did not improve.

One patient was anxious to do anything to get well, as quickly as possible. So, finally, Dr. William Hinton performed sympathetic surgery on the patient, cutting the distal rami of the second, third, and fourth dorsal ganglia. In the same patient he also performed a scaleniotomy and ruled out an anomalous subclavian vein running under, instead of over, the scalenus anticus muscle. (In that way compression of the vein and venous obstruction might be produced.) Both these procedures were carried out on the patient, but two months later her clinical picture seemed to be following the same course as that of the other cases.

If we are going to consider a disordered sympathetic nerve supply as the cause of trouble, as in causalgia and Sudeck's atrophy, there should be evidence of vasospasm or of vasodilatation. Our patients did not present quite the symptoms of those groups of cases as described in the literature, though it is possible we did not study our cases minutely enough to make any positive differentiation.

Dr. Kerr brought up the question of Oppenheimer's syndrome. Our patients did not suffer from neuritic symptoms, but all presented shoulder pain and disability. Only two of them showed any appreciable degree of cervical osteo-arthritic changes.

On the question of shoulder or hand involvement, or both, following coronary occlusion there is no doubt about their occurrence. We see such involvement in older patients after various illnesses—pneumonia, Parkinson's syndrome, or other conditions, as well as myocardial infarction—imposing a bed-fast period. However, isolated involvement of the shoulder or hand in these ailments, and even " post-infarction sclerodactylia ", differ from the syndrome just described in one respect. All our patients were ambulatory and in good general health, and most of them were working hard.

Dr. Freyberg's remarks were quite appropriate. The differential diagnosis from rheumatoid arthritis apparently contributes the most frequent source of confusion. It is important not to treat this disorder as rheumatoid arthritis.

Dr. Rosenberg referred to a number of other conditions, of which we are aware, that deserve the emphasis he gave them. In the literature there is a miscellaneous group of patients who fall within this category. We have found to our great surprise practically no specific reference to this particular clinical picture. Occasionally it is suggested in passing that a patient with a painful shoulder may show swelling of the hand.

In summary, I have presented six patients with painful, homolateral disability of the shoulder and hand with swelling and atrophy of the hand. The syndrome, as far as we could tell, was not cardiac or traumatic in origin, and in at least four of these patients there was no demonstrable cervical osteo-arthritis.

DYNAMIC POSTURE

BECKETT HOWORTH
New York

Dr. Howorth said that posture was usually described as an inactive position of standing or sitting. This should be called static posture. Posture should really be considered as all the various positions of the body throughout the day and throughout life, including the positions of lying, sitting, and standing, and the transitions between these positions, and all the motions and actions of the body. Good posture was usually described as the most erect standing or sitting position. Such posture had certain advantages but was useless for action.

Dynamic posture was posture in motion, or in action, or in preparation for action. This was a new term, and it was suggested that it be adopted for general use. Dynamic posture was a part of our everyday lives, but the field was almost completely unexplored. Dynamic posture included the transitions between the various static postures, and also walking, running, jumping, climbing, dancing, swimming, and all our activities both at work and at play. The basic dynamic position was a crouch, with hips, knees, and ankles flexed, this being quite different from " poor posture ". It provided the maximum advantage in body balance and mechanical advantage for the muscles. The muscles also acted as springs, absorbing physical shocks and preparing for ensuing actions, in the basic dynamic position.

Dynamic posture used all the elements of effective musculo-skeletal performance. Muscles contracted, but they should also relax, and good performance in action usually depended upon the smooth alternation between contraction and relaxation. Rhythm and co-ordination contributed to this smooth action. Balance was essential to good dynamic posture; the weight was usually centred over the active foot. Sometimes the inertia of the trunk might be used for balance or for resistance. Momentum might be a powerful factor in dynamic posture. Finally, timing was the most delicate factor of all, and one of the most essential. The smooth integration of these elements of dynamic posture resulted in physical performance which was simple and easy, less tiring, satisfying, graceful, and effective.

DISCUSSION

DR. ROBERT B. OSGOOD (Boston): I agree with what Dr. Howorth has said. In making patients assume good postures, I have found it practical first to know if the lumbosacral joint is movable, and that is easy enough to find out by radiographs in different positions—and then to teach them how, leaving their shoulders free, to continually pull in the lower abdomen.

DR. JOHN G. KUHNS (Boston): It is worth mentioning that thirty years ago a woman doctor in New York City, Dr. Bess Amenstenti, wrote a book advocating functional gymnastics for women, and she had exactly the same type of argumentation as we heard to-day.

THE DIAGNOSTIC SIGNIFICANCE OF FOCAL CELLULAR ACCUMULATIONS IN THE SKELETAL MUSCLES OF PATIENTS WITH RHEUMATOID ARTHRITIS

G. K. DE FOREST, H. BUNTING, and W. E. KENNEY
(INTRODUCED BY J. R. PAUL)

These authors described how muscle biopsies were done on sixteen cases of rheumatoid arthritis in an effort to repeat the work of Freund[1] and his collaborators. As controls, biopsies were done on fifteen other patients, among whom were included cases of osteo-arthritis, rheumatic fever, gonococcal arthritis and " non-specific infectious " arthritis; similar studies were made on twenty-two routine autopsy cases. Muscle lesions were found in twelve of the sixteen cases of rheumatoid arthritis and in two of the four control cases of "non-specific infectious" arthritis. With the exception of one patient with osteo-arthritis, who had a history suggestive of rheumatoid arthritis, these lesions were absent from all other controls. The results gave no indication of any fundamental difference between the " atrophic " and the " non-specific infectious " forms of rheumatoid arthritis.

The lesions consisted of focal accumulations of lymphocytes and macrophages occurring either in perivascular locations in the perimysium or in the endomysium between the individual muscle fibres. Hyalinization, vacuolization, loss of striations, and atrophy of muscle fibres were found frequently in association with these cellular foci in the above group, while in the controls similar degenerative changes occurred without any cellular reaction.

No direct correlation could be found between the presence of these lesions and the duration or activity of the disease, nor were they related to previous gold therapy.

DISCUSSION

DR. WALTER BAUER (Boston): Dr. Raymond Morrison of our group has found similar lesions in one case each of lupus erythematosus disseminata and dermatomyositis. Was more than one biopsy done on any one patient? (Dr. James F. Rinehart also said he had seen several instances of a comparable reaction in disseminated lupus.)

DR. OTTO STEINBROCKER (New York): This subject represents one of the most promising advances in our understanding of the pathology of rheumatoid arthritis. It certainly confirms what Dr. Freund has published. Have these lesions been found in other conditions? Was there any difficulty in recognizing them? We have tried to find them for some time through our pathology department.

In the discussion three cases of negative rheumatoid arthritis were mentioned. Two of these were of Marie-Strümpell disease, if I understood correctly, presumably with peripheral joint involvement. I doubt if they would fall within the accepted classification of true rheumatoid arthritis. The distinction had better be made clear as to exactly in which diseases we may expect positive and negative results.

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[1] *Science*, 1945, **101**, 202.

DR. RICHARD H. FREYBERG (New York): The fact that these focal cellular collections occur early in the course of rheumatoid arthritis can be attested by two patients that we saw in the very early states of their disease, at which time we were in doubt as to whether they had rheumatoid arthritis. They were studied by Dr. Hugo Freund within one or two months after we saw them, and at that time they had focal cellular collections in muscles. Later the course of their disease was characteristic of rheumatoid arthritis.

DR. GIDEON K. DEFOREST (closing): The biopsies were arbitrarily taken from the bellies of the deltoid and gastrocnemius muscles. We did not take them necessarily from muscles near involved joints. In all our cases of rheumatoid arthritis, biopsies were taken from both the deltoid and gastrocnemius muscles. I am sorry not to be more familiar with Dr. Selye's work, but I am quite sure our findings are not the same. His histological studies, I think, were limited chiefly to the myocardium and periarticular structures.

We had little difficulty in finding these changes. We did turn over the blocks of tissues in our negative cases and cut sections from the other side. In one of our original negative cases we were able to demonstrate the changes by this means.

I think these findings are further evidence that there is little reason for separating non-specific infectious arthritis from rheumatoid arthritis with predominantly atrophic changes.

THE STREPTOCOCCUS SEROLOGY OF RHEUMATOID ARTHRITIS

ALLAN D. WALLIS

Philadelphia

Dr. Wallis said that serologic specificity did not require that a test antigen come from the same source as its corresponding immunizing antigen, provided they have a reactive area or chemical surface configuration in common, e.g. Wassermann reaction, Weil-Felix reaction. The occurrence of agglutinins for haemolytic streptococcus in the serum of rheumatoid arthritis had been interpreted as showing that haemolytic streptococci were the cause of the disease, but there was serologic and clinical evidence against this interpretation; serologically, the antistreptolysins and antifibrinolysins which accompanied frank streptococcal disease were absent; clinically, the chronicity of the active stage of the disease, the symmetry of the lesions, and their indifference to sulphanilamide or penicillin argued against an infectious origin. In arthritis serum precipitins had been found against the following fractions of Group A haemolytic streptococcus: (1) the group-specific C-carbohydrate, (2) nucleoproteins, (3) a non-protein fraction which was tentatively designated Z. Anti-C would account for nucleoprotein precipitation, inasmuch as the nucleoproteins had been shown by Heidelberger to contain C. We had serologic evidence that anti-C would not precipitate Z. Hence there were at least two antibody types in arthritis serum. We had serologic evidence that the anti-C and anti-Z precipitins were both eligible to serve also as agglutinins. Hence these two antibody types would account for all the known serologic reactions of rheumatoid arthritis serum with Group A haemolytic streptococcus and its fractions.

Rheumatoid arthritis serum agglutinated suspensions of fine collodion particles. This appeared to be a non-specific flocculation. It was due in part to the presence of anti-C and anti-Z. The increased ability of arthritis serum to agglutinate the non-encapsulated pneumococcus was apparently a non-specific enhancement of the action of normally present antibodies against pneumococcus fractions.

It was suggested that the antigens which aroused anti-C and anti-Z might be produced, without the intervention of bacteria, by a perversion of the normal synthesis of the lubricating mucopolysaccharide hyaluronic acid by the synovial cell. The capsule of the Group A streptococcus was also composed of hyaluronic acid, which in this case was probably not polymerized in the same manner as in synovial fluid. Dr. Wallis proposed the hypothesis that in rheumatoid arthritis the synthesis of hyaluronic acid by the synovial cell was diverted into the biochemical channels followed by the Group A haemolytic streptococcus in its hyaluronic acid metabolism.

Discussion

Dr. Russell L. Cecil (New York): Those of us who were working with these agglutinins in the early days of course entertained the possibility of their being non-specific in nature, and it was always a source of disappointment that patients who showed these very high agglutination reactions in their sera so frequently showed no streptococci in the joints or blood stream nor in the buccal cavities, stools, or any part of their bodies. One would naturally expect that if we were dealing with a chronic streptococcus infection the offending streptococcus could be found somewhere to account for these agglutinins; hence the non-specific theory had to be seriously entertained.

Dr. Wallis has given us a very interesting hypothesis to think about, but I feel that we should not be too quick to dismiss the Group A haemolytic streptococcus entirely from the aetiology of rheumatoid arthritis, especially when we remember what an important rôle this organism plays in rheumatic fever, and how comparatively frequently we see cases which are borderline between rheumatic fever and rheumatoid arthritis.

A great deal has been written about the close relationship, clinically and perhaps aetiologically, between rheumatic fever and rheumatoid arthritis, and for that reason I think we ought to at least keep in the background the possibility of some relationship between the haemolytic streptococcus and this disease.

Are these collodion particles agglutinated by antipneumococcus serum of specific types?

Dr. Ralph H. Boots (New York): The first observation on the streptococcus agglutination in rheumatoid arthritis was not made by Dr. Dawson, Miss Olmstead, and myself, but by Drs. Nicholls and Stainsby. We did not believe this reaction at first, and it was only by collaboration with their group that we were able to assure ourselves that it actually existed. While this paper of Dr. Wallis's throws some light upon it as a non-specific agglutination, yet I agree with Dr. Cecil that one should not, at this time, entirely disregard the possibility of its being a specific reaction.

Dr. John R. Paul (New Haven, Conn.): Dr. Wallis mentioned that hyaluronic acid was present in Group A streptococci; did he consider that hyaluronidase also was present in some strains of haemolytic streptococcus, and that that also entered the picture?

Dr. Abraham S. Gordon (Brooklyn, N.Y.): What studies, if any, were made on the serum protein, and what were the results of such studies ?

Dr. P. F. De Gara (New York): How often do you find those agglutinations? In other words, is there a correlation between the number of cases in whom you find *Strep. viridans* and the number of cases where you find agglutination of collodion particles?

DR. HOWARD C. COGGESHALL (Dallas, Texas): I have worked with collodion particles and found that there are many instances of non-specific agglutination. It depends on the *p*H of the solution, the content of chloride and sodium, and so on. Did the author find that by manipulation he got auto-agglutination?

The point was made that there is a relative hyperglobulinaemia in many of these cases. I wondered if the author has done any of these tests on people of known hyperglobulinaemia. We have not found positive agglutinations in people with other conditions where there is a high globulin.

DR. HERMAN H. TILLIS (Newark, New Jersey): Has the type of globulin been differentiated?

DR. OSCAR SWINEFORD (Charlottesville, Virginia): We have worked with the collodion particles, and I second the statement that there has been a good deal of non-specific agglutination. Were Dr. Wallis's experiments conducted with sterile technique throughout? Of all the things we tried—and we have done more than two thousand experiments with the collodion particles—contamination of human serum gave us the strongest agglutinations.

DR. ALLAN D. WALLIS (closing): We have purposely avoided borderline cases and difficulties of diagnosis. The problem is tough enough if you can stick to the typical cases in which there is no question of diagnosis. If we can get an answer for the typical ones—the ones that we can recognize across the street-car and make a diagnosis—that will be a start.

We have mulled over the question of hyaluronidase, and as far as I can see there is no relation to the problem at hand. We became interested in the relation of hyaluronidase in the streptococcus, and our impression is that there is probably a hyaluronidase inhibitor in the streptococcus capsule. The capsule disappears suddenly when the organism is about six hours old. The hyaluronidase presumably was there all along. What protected the hyaluronic acid of the capsule from the enzyme? I would guess an inhibitor. That is a side issue. I don't think it has any relation to the problem of rheumatoid arthritis.

We have made no determinations of serum protein fractions. The results I quoted were those of Davis and of Pemberton and his associates.

On the question of the incidence of the ability to agglutinate collodion particles, we have had considerable difficulty in securing uniformity of batches, which makes it hard to reproduce results quantitatively. We did not think it was a very pleasant method to work with. But in general, we controlled each batch of collodion particles, and I must say that some of them were not agglutinated by strong arthritis serum. But those which were, the agglutinable batches, were controlled with normal sera, and I have no question in my own mind that the agglutination of suitable batches of collodion particles by strong arthritis sera is a genuine reaction. We made no attempt at sterility in our collodion technique, but again we felt that the normal controls covered that satisfactorily. We did not try out antipneumococcal sera against collodion. If the patient had hyperglobulinaemia I would expect a positive reaction. Some other discussers have said they have tested serum of patients with high globulin from other disease states and found no agglutination of collodion particles. That is interesting. As to the fraction of globulin concerned, I have no information.

ADDENDUM

Some of the concepts expressed in the abstract of Dr. Wallis's paper have subsequently been revised (see *Amer. J. med. Sci.*, 1947, **213**, 87 and 94).

CARDIAC LESIONS IN RHEUMATOID ARTHRITIS

EDWARD F. ROSENBERG, LOUIS F. BISHOP, HENRY WEINTRAUB, and PHILIP S. HENCH

The above four workers pointed out that, although in classic instances the clinical and pathological manifestations of rheumatoid arthritis and rheumatic fever were strikingly different, in some cases the one could not be distinguished from the other. This difficulty resulted from the fact that many clinical features were common to both diseases. In borderline cases the distinguishing features might not be discernible.

There had been wide acceptance of the concept that carditis was a regular accompaniment of rheumatic fever but did not occur frequently in patients with rheumatoid arthritis. However, recent studies indicated that serious cardiac lesions which were not distinguishable from those caused by rheumatic fever could be found at necropsy in a rather high percentage of individuals with rheumatoid arthritis. In four such studies, conducted at different centres by independent observers, the incidence of such carditis among patients dying with rheumatoid arthritis was found to be 26 to 65%. These surprising results led to the present study, in which the authors reviewed in detail the character of clinical and laboratory findings as regards cardiac disease in 147 patients with proven rheumatoid arthritis. The observations on these patients were compared with similar observations on 100 normal individuals. The data considered included the results of auscultatory and sphygmomanometric studies, radiographic examinations of cardiac contours, and a detailed analysis of electrocardiographic tracings. The incidence of rheumatic heart disease judged on the basis of bedside evidence was not notably higher in the arthritic group than among the controls.

Dr. Louis Faugeres Bishop, Jr. (New York), one of the workers in this study, said that they had made some steps forward but would like to say a word or two about the method. In the first place, they were cautious in interpreting their electrocardiographic findings, the present normal standards being almost too rigid. They adopted the normal standards of Dr. Katz of Chicago, which were fairly liberal. Unfortunately the opportunity for making serial tracings arose only with one patient, and care was needed to say what one electrocardiogram showed. In the evaluation of any electrocardiogram it was important to remember that a normal tracing did not rule out heart disease, and an abnormal one did not necessarily indicate heart disease. It was unfortunate that all the patients were not fluoroscoped, because minor degrees of cardiac enlargement are frequently discovered by fluoroscope and by no other means.

They had been particularly careful in examining murmurs, examining only a few every day and making sure that none of the examiners was tired. They had listened carefully in all positions, using two types of stethoscope, the ordinary

Bell, and the Bowles, and particularly looking for a type of murmur which is frequently overlooked, the aortic diastolic murmur without associated cardiac findings—of which only one case was found in the entire series. So with their present methods of examination their cardiac findings did not agree with what had been found at autopsy in this group of cases.

Discussion

Dr. Russel J. Cecil (New York): An analogy could be drawn between these interesting reports: that is, infiltration of the muscles with lymphoid cells, plasma cells, and the infiltration of the heart muscle and of the valves. A distinction should be drawn, though, between functional and anatomical heart lesions. In other words, these rheumatoid patients have pretty good hearts so far as function goes. It seems that the interest here is a theoretical one. It shows that rheumatoid arthritis is a systemic disease, characterized by infiltrations not only into the synovial membrane and other joint tissues, but also into the muscles, nerve sheaths, and heart muscles; but clinically and practically I think it is amazing how little trouble the average rheumatoid arthritis patient has with his heart.

Dr. Philip S. Hench (Rochester, Minnesota): When in 1940 Drs. Rosenberg, Baggenstoss, and I first studied the necropsy specimens of the hearts of patients who had had rheumatoid arthritis and noted a high incidence of cardiac lesions, we asked Dr. Willius, Chief of the Section on Cardiology at the Mayo Clinic, to review with us the cardiac status of all the rheumatoid arthritic patients then on the rheumatism service. Their disease had averaged about six or seven years in duration; it was not in an early stage. Although this study was made rather informally we found no more clinical evidence of heart disease in the living rheumatoid arthritic patients than has been reported to-day in the study on soldiers.[1] Thus, the hearts of most living rheumatoid arthritic patients appear to be quite normal so far as current clinical methods of examination permit one to determine, even though the hearts of most dead rheumatoid arthritic patients reveal disease.

Dr. R. M. Stecher (Cleveland, Ohio): Was the diagnosis of rheumatoid disease made on all cases before they came to autopsy?

Dr. E. F. Rosenberg (closing): In many instances we found advanced lesions with tight mitral stenosis and other changes characteristic of rheumatic heart disease. All who have studied this problem have been impressed, as we were, that these patients have advanced rheumatic cardiac lesions at necropsy. The diagnosis of rheumatoid arthritis was made before death by physicians especially trained in the study of rheumatic diseases. There was no doubt in our minds as to the accuracy of the diagnosis.

PRECIPITATING AND PREDISPOSING FACTORS IN RHEUMATOID ARTHRITIS

J. OWEN FINNEY, EDWARD W. BOLAND, and PHILIP S. HENCH

A study was presented in which 100 male soldiers with rheumatoid arthritis were investigated to discover factors which might have served to precipitate the onset or predispose to the development of the disease. A history of the presence of some factor which might have precipitated an initial attack or a relapse of the

[1] *Proc. Mayo Clin.*, 1941, **16**, 237.

disease was obtained in forty-two of the one hundred patients, was questionably present in eleven, and was not obtained in the forty-seven remaining patients. Thus, although certain factors may apparently serve to precipitate the onset or a relapse of rheumatoid arthritis, the presence of such could not be considered a prerequisite for the appearance of symptoms in this series.

Of the forty-two patients in whom some factor appeared to have been significantly related to the onset of rheumatoid arthritis, the history of an infectious process was obtained in twenty-one, exposure in twelve, physical joint trauma in five, physical fatigue in two, psychic trauma in one, and a surgical operation shortly preceded the onset in the one remaining. Thus, an infectious process appeared to be the most significant of the factors considered as a probably precipitating mechanism of rheumatoid arthritis in this series. A specific or non-specific genito-urinary tract infection was the factor held responsible in more than one-half (gonorrhoea seven, non-specific genito-urinary infection four of the cases in which an infectious process was apparently related to the onset of the disease. These workers considered that infections of the genito-urinary tract, especially gonorrhoea and non-specific urethritis, have failed to receive their due consideration as agents which may precipitate rheumatoid arthritis.

It appeared that exposure served as one of the factors which might precipitate an initial attack or a relapse of rheumatoid arthritis in soldiers. However, the maximum exposure to which an individual had been subjected was not necessarily that related to the onset of the disease. In view of the information that no case of rheumatoid arthritis was encountered in more than 1,200 soldiers who had been subjected to exposure of sufficient severity to result in trench foot, it appeared that this factor was not provocative in the absence of individual susceptibility to the disease. That joint trauma (particularly repeated microtrauma) might play a greater rôle as a precipitating factor than was indicated by the results of this study were suggested by the fact that in eighty-two of the one hundred soldiers the joints of the lower extremities were first involved. Physical fatigue apparently may serve as one of the infrequent precipitating factors of rheumatoid arthritis. With the method employed in this study, psychic trauma did not appear to be significant as a precipitating factor of rheumatoid arthritis; having been recognized in only one case. In one patient rheumatoid arthritis was apparently precipitated by a surgical operation.

It was interesting that a history of some factor which might have acted as a precipitating agent of rheumatoid arthritis was obtained in 66% of the patients, while in only 36·5% of those with an initial attack of the disease was the history of a precipitating factor elicited. These factors, then, appeared more significant in provoking a relapse of rheumatoid arthritis than in precipitating an initial attack.

Factors which had reportedly served to predispose an individual to the development of rheumatoid arthritis (heredity, body habitus, dietary imbalance, allergy, geographic environment, climate, and occupation) were not considered to have contributed directly to the onset of the disease in any of these one hundred patients.

Geographic environment, climate, and occupation presumably might be of such nature as to subject an individual to certain of the predisposing factors discussed. Twenty-four of the patients gave a history of the presence of some rheumatic disease in one or more relative, none of whom were examined. A conclusion that a hereditary or familial influence was important in the production of rheumatoid arthritis in the subjects examined was not warranted.

In 60% of the soldiers in this series who had experienced an initial attack of rheumatoid arthritis before entry on active duty, a relapse occurred within the first year of service; while only 18% of those in whom the initial attack of the disease occurred after beginning active duty became ill during the first year of service. From this it appeared that military service was particularly hazardous for an individual who has had rheumatoid arthritis.

Discussion

Dr. Wallace Graham (Toronto): In 5% of the 100 cases, trauma was considered the precipitating factor. This is a very significant figure in provinces such as ours, where the Workmen's Compensation Board is responsible for all medical costs related to an injury while at work. Recently I have seen two cases of rheumatoid arthritis with onset after a blow on the knee: there was no evidence of preceding joint disorder in either case. The Compensation Board is naturally loth to accept full responsibility for a chronic systemic disease which followed trauma. To what degree they should be responsible can only be determined by more reports such as the ones we have just heard. I would like to hear a few more details about the traumatic cases.

Dr. Charles L. Short (Boston): I would be in general agreement with the figures that have just been presented, except that we did not find as many cases in the Mediterranean Theatre following infection; in fact, there were only a small number. I think the reason for that is that we had these patients under observation for a short time, and there was some doubt in atypical cases—perhaps following dysentery or gonorrhoea—as to the true nature of the disease. That may have led me to throw out a number of cases which might later have developed typical rheumatoid arthritis.

I would agree that the hardships overseas could not be termed causative factors in the patients I saw; that at least half of them gave a history of having had arthritis clinically compatible with rheumatoid arthritis before being inducted, and about two-thirds gave a similar history before they had gone overseas at all. Somehow or other these soldiers escaped the screening of the induction board and of the ports of embarkation. In fact, some of them were sent over with the statement that they were going to Africa and that was a good climate for them and their joint symptoms would probably improve. When they arrived in North Africa, many of them developed full rheumatoid arthritis. In the soldiers that I saw in the Mediterranean Theatre, a large number of them developed either the first attack of the disease or an exacerbation within two months after landing overseas. This suggested some relationship between the differences in life in the States and life in the field. Just what that was, whether it was exposure, or the anxiety of being overseas, I do not know and I do not think it would be possible to analyse. I certainly was not struck by any soldiers whose disease started directly following combat experiences. In fact, I remember one soldier who, as long as he was up in the mountains in the winter, felt fine; and then when he came down to the warm plains in the base section in the spring, his rheumatoid arthritis flared up.

Dr. Philip S. Hench (Rochester, Minnesota): Drs. Finney, Boland, and I would like to acknowledge our indebtedness to Lieut.-Col. Philip Lewin and to Major Thomas J. Dry for giving us their figures on the lack of incidence of rheumatoid arthritis among patients who had

trench foot. Among their combined 1,200 cases of trench foot no case of rheumatoid arthritis developed. That is an interesting observation when one considers the supposed factor of damp and cold in the production of rheumatoid arthritis.

This study reminds me of the studies on rheumatic fever by Dr. Swift and others who have, during recent years, shifted the emphasis from physical exertion to infection as a major provocative cause of recurrent rheumatic carditis and decompensation. It used to be thought that patients who had rheumatic carditis should be "wrapped in cotton" and not allowed to work. Now it is known that it is more important for them to avoid certain infections than to avoid physical exertion.

Before some of us went into the Army, we were told by friends: " Of course you will see lots of rheumatism in the Army from the exposure of soldiers to the wet and cold of trenches and field warfare". In this study we did find evidence that exposure sometimes served as a provocative for rheumatoid arthritis, but not nearly as often as we had anticipated and not nearly as often as did infections. Of special interest was our finding that acute genital (not articular) gonorrhoea was a notable provocative of rheumatoid arthritis. This is not an entirely new fact. Those of experience have from time to time noted such cases in civilian practice. Dr. Pemberton during World War I noted that in 1% of four hundred soldiers who had " chronic arthritis " the arthritis came on in close relationship with the onset of gonorrhoea, and in 8% of his civilian male arthritic patients a similar relationship was obtained, a relationship which we found in 7% of our 100 cases of rheumatoid arthritis among soldiers.

One hundred cases of rheumatoid arthritis, studied in relation to provocative factors, may seem to some like a small and inadequate number, but such a study is more difficult than one might think, as it demands close and critical questioning and evaluation.

Dr. Edward W. Boland (Los Angeles): This paper emphasizes the distinction between aetiology and precipitating mechanisms. Too often physicians are inclined to think of trauma, infection, exposure, and so forth as the actual causes of rheumatoid arthritis, whereas it is probable that such factors, at best, merely serve to bring the disease into light clinically. The fundamental cause of rheumatoid arthritis is not known. Trauma, various infections, exposure, etc., may be looked upon as " trigger " mechanisms: the patient is probably already silently " charged " with the disease and when one of several " triggers " is pulled the clinical manifestations are set off.

Dr. J. O. Finney (closing): The evaluation of the nutritional status of the patient was done on a purely clinical basis. There was no clinical evidence of any dietary deficiency in the individuals. Sixty patients gained weight. We did not find any of those to have clinical evidence of oedema. In thirty-three the weight had been reported constant from the time of admission into the Army until the time of onset of the illness. Only seven patients had lost weight before the onset of the illness or the onset of the relapse, and five of these had been obese at the time of entry on active duty. No laboratory studies relative to the nutritional status of the patients were made.

Trauma was considered a precipitating factor in 12% of the forty-two cases in which a precipitating factor was thought to be present, but in only 5% of the total of the one hundred cases. Three of those cases were instances of what we might call micro-trauma following long marches and two followed a direct blow: one a direct injury to a joint, a sprained ankle, the other the falling of a heavy weight on the joint. The injured joints were involved initially; then the diseases spread to other joints of the body.

RHEUMATOID SPONDYLITIS: A STUDY OF 1,035 CASES

HOWARD F. POLLEY and CHARLES H. SLOCUMB
Rochester, Minnesota

Rheumatoid spondylitis, according to these workers, occurs in males and females in a ratio of 9 : 1. The average age at the onset of symptoms was 26·7 years; 80% of the patients were from fifteen to thirty-five years of age. The average duration of symptoms before examination was 8·5 years. The first symptoms were in the torso in 72%; in the neck and shoulder girdle in 3%; and in the peripheral joints in 23%.

Limitation of movement in the cervical portion of the spinal column was noted in 45% of cases. Involvement of the hip joints was found in 28%, the damage to the hip joint being bilateral in three-fourths of these cases. Symptoms referable to peripheral joints were found in 50% of the cases of rheumatoid spondylitis, but in only 25% did it lead to chronic residual articular damage. The sedimentation rate was normal in a fifth of the cases, and was less than 60 mm. (Westergren method) in about three-fourths.

The characteristic radiographic findings in rheumatoid spondylitis are arthritis of the sacro-iliac and apophyseal joints, calcification or ossification or both of spinal ligaments, and osteoporosis of vertebrae. Bilateral sacro-iliac arthritis was a characteristic and relatively early feature of rheumatoid spondylitis. It occurred in 98% of cases.

DISCUSSION

DR. RICHARD H. FREYBERG (New York): This is an excellent study of a large group of cases of spondylitis from which I think we all should learn a great deal. Were any differences observed in the incidence of involvement of the upper part of the spine in relation to the age of the patients? Is there a greater incidence of high-back involvement, with less or no low-back involvement, in the older age group? How many patients were found that had true arthritis in the shoulders in contradistinction to those who had stiffness and limitation of motion not due to arthritis but due to muscle, tendon, and other soft-tissue involvement about the shoulders?

I would like to stress the fact that Dr. Polley reported that slightly less than 1% of the cases studied showed no sacro-iliac involvement by *x* ray; also, Dr. Polley's concluding statement that any patient, especially if he is a young male, who claims to have back or leg pain, should have diagnostic radiographs, including pelvis films, to show sacro-iliac joints to good advantage.

How many of these patients had hereditary or family incidence? We have been impressed that a large percentage of patients with spondylitis tell of their brothers, fathers, or sons who have true spondylitis. Oftentimes it is not recognized. We have studied families of patients and found, to the surprise of the individual concerned, that a brother or a father or a son of the patient we first saw had spondylitis, and that he had back pains often for years and nothing had been done about it. In one family, the father and three sons had spondylitis with typical radiographic evidence. One son had no sacro-iliac involvement; the disease was confined to the dorsal and lumbar portion of the spine. Another son had the more characteristic involvement, the arthritis beginning as sacro-iliitis and later ascending to involve the lumbar and dorsal spine. A third son had cervical and dorsal spondylitis only. We found families in which the female sex was

affected also—father and daughter, or a son and his mother would have spondylitis. The possible hereditary factor and the family incidence of this disease needs to be studied further.

DR. EDWARD W. BOLAND (Los Angeles): Dr. Polley's study is of particular interest to those of us who were connected with Army rheumatism centres. Rheumatoid spondylitis was one of the most common types of rheumatic diseases encountered among soldiers. Of the first 7,000 consecutive admissions to the centre at the Army and Navy General Hospital, 1,274 cases of rheumatoid spondylitis were encountered; thus, about one out of every five soldiers admitted had this disease.

We have been able to carry out several clinical studies on these patients. One study was similar to Dr. Polley's, and many of our findings were statistically similar to his. We also found that the first symptoms were usually located in the lower back; that almost always the first radiographic changes occurred in the sacro-iliac joints; that approximately one-fifth of the cases had associated involvement of peripheral joints; that hip and shoulder involvement was not frequent early in the disease; that the radiographic changes and the clinical course seemingly were identical, regardless of whether peripheral joints were or were not concomitantly involved; that gonorrhoea was found in association with the onset no more frequently than in patients with peripheral rheumatoid arthritis.

We have attempted to classify our cases on the basis of disease severity, such classification being based on the rate of progression of the disease, the amount of constitutional reaction, the height of the erythrocyte sedimentation rate, and the degree of disability presented. Using such criteria, we have found that the severity of the disease is often reflected by the radiographic characteristics of the sacro-iliac changes (if studied before ankylosis has occurred). When the disease is mild, subchondral sclerosis and narrowing of the joint space are the dominant features. When the disease is moderate in severity, subchondral rarefaction and sclerosis are present in fairly equal proportions and joint mottling is definite. When the disease is severe, subchondral rarefaction and joint destruction are extreme, but sclerosis is rarely conspicuous.

Dr. Polley brought out the fact that when peripheral joints (also) are involved in patients with spondylitis, there is a decided preference for the joints of the lower extremities; our experience confirms this observation. The predilection for initial joint involvement in the lower extremities, especially in the metatarsophalangeal joints and the knees, may be a sex peculiarity rather than a peculiarity of spondylitis. In approximately 75% of our soldiers with peripheral rheumatoid arthritis (without associated spondylitis), the first joints involved were those of the lower extremities. This is in contrast to the predilection for initial upper extremity joint involvement in females.

Regarding Dr. Freyberg's remarks on the radiographic findings in spondylitis, I think we all agree that unequivocal diagnosis cannot be made without positive radiographic findings, especially in the sacro-iliac joints. But, just as in rheumatoid arthritis involving the peripheral joints, the disease may progress for months or even years before radiographic manifestations become evident. One should be cautious in discarding the possibility of early spondylitis because of the lack of sacro-iliac alterations; the radiographs may not show positive changes for two to three years after the onset.

Dr. Polley's original thesis contained information regarding pathologic data which was not mentioned to-day. Dr. Polley was able to study microscopic sections taken from peripheral joints (in patients with spondylitis). In view of the paucity of pathologic data in this disease, we would appreciate hearing the results of this study.

DR. JOHN G. KUHNS (Boston): What were Dr. Polley's criteria for early diagnosis? In the younger age group, particularly that group which Dr. Scott calls juvenile spondylitis, diagnosis in the early stages is very difficult. There are many infectious processes which you have to consider. We have seen a number which I thought were going to develop spondylitis and then found they got well. Of course the calcification of the ligaments and fusion of the sacro-iliac joints are frequently part of a healing process in late stages of the disease. We have also seen a number

of quiescent fusions of the sacro-iliac joints. Has Dr. Polley seen any patients who have given no symptoms whatever of spondylitis?

Another interesting point is the incidence of peripheral arthritis as an early symptom: was there more in women than in men? We have found it predominantly in women.

DR. R. M. STECHER (Cleveland, Ohio): Would Dr. Polley say a word about the type of arthritis which involves the hips in patients with rheumatoid spondylitis? We all agree that this type of arthritis of the spine is essentially a manifestation of rheumatoid arthritis, or rheumatoid-like arthritis, but it seems that very often changes which occur in the hips have radiographic appearances indistinguishable from degenerative joint disease. There is no demineralization, there is decrease in joint space, and a production of spurs large enough to cause complete ankylosis due to bony block without true bony fusion. I have seen fusion occur, too, but ordinarily the manifestations are those of degenerative joint disease.

DR. EPHRAIM P. ENGLEMAN (San Francisco): Some of the patients admitted into rheumatic fever centres later turned out to have peripheral rheumatoid arthritis. It was of great interest to us that approximately one-third of those patients in whom a diagnosis of atypical rheumatoid arthritis was made showed radiological signs of rheumatoid spondylitis. Two things are of particular interest in relation to this group of cases: first, many of these patients had very few, if any, symptoms referable to their back; and secondly, about a quarter, had demonstrable lesions of the heart which we presumed to be due to coincident rheumatic heart disease. What, if any, studies has Dr. Polley undertaken on the possibility of coexisting heart disease in spondylitis?

DR. ROLAND DAVISON (San Francisco): How often has Dr. Polley seen patients with involvement of the sacro-iliac joint and in the cervical spine without involvement of the dorsal and lumbar spine? We have had two cases in the past year. Do his female cases show any distinguishing characteristics physically?

DR. DOUGLAS TAYLOR (Toronto): It seems generally accepted that in so-called " rheumatoid spondylitis " the essential lesions are in the sacro-iliac and apophyseal (intervertebral) joints. One wonders if radiographs of these two sets of joints were taken, particularly the oblique films to show the lumbar facets; and especially in the early cases. Frequently in early cases the only changes to be found are in the sacro-iliac joints, and the disease may become arrested at this stage of sacro-iliitis. Are we justified in diagnosing these early cases as " spondylitis " when there is no evidence of involvement of the spine? With our present knowledge of this syndrome the term " Marie-Strümpell " seems to have fewer disadvantages than the term " rheumatoid spondylitis ".

DR. H. F. POLLEY (closing): The average age of patients whose symptoms of rheumatoid spondylitis started in the upper part of the back is slightly higher than the average age of those whose symptoms started in the lower part of the back, but the difference is not statistically significant. There would seem to be a greater possibility of seeing patients in the older age groups without involvement of the lower part of the back than in the younger age groups, but I have no statistics to support this impression.

Criteria for involvement of the shoulder were pain and limitation of motion of the shoulder and functional disability. We did not prove the presence of intra-articular damage in all cases in which involvement of the shoulder was described; we did, however, find characteristic evidence of rheumatoid arthritis in one case, to which I shall refer in a moment.

We encountered several interesting family histories similar to those Dr. Freyberg has described. The possibility of hereditary predisposition to rheumatoid spondylitis is indeed an interesting subject. I suspect that the incidence of a family history of rheumatoid spondylitis may be greater than our figures would indicate, but in this study we found a definite family history of the disease in only 0·4%.

Symptoms referable to peripheral joints at the onset of rheumatoid spondylitis were predominantly in joints of the lower extremities, but when peripheral joints were involved later in

the course of the disease there was no predominance of involvement of the joints of the lower extremities.

In this study there were included only those cases in which a definite diagnosis of rheumatoid spondylitis could be made. The problem of criteria for early diagnosis did not seem applicable in this phase of our study. It is a very important question, and we hope that our data may help in some way to answer the question more satisfactorily.

The so-called antecedent rheumatism which is thought by some to characterize the onset of rheumatoid spondylitis in many instances was found to be a very infrequent feature of the history of the patients in this series. There were five patients in the 1,035 studied who had had no symptoms of rheumatoid spondylitis. In these patients the diagnosis was made on physical examination and on radiographic evidence of the disease.

Dr. Stecher asked about the nature of involvement of the hip joint. Since the hip joint is a weight-bearing joint, it is perhaps more susceptible to the changes of a degenerative (osteo-arthritic) type if it has already been subjected to the changes of an inflammatory (rheumatoid) character than if it has not been subjected to these changes.

Dr. Boland has referred to a phase of this study which we could not include in our paper at this time. Biopsy of synovial membrane was performed in some of the cases of rheumatoid spondylitis with involvement of peripheral joints. In about half the cases in which we were able to obtain biopsy material the operation was carried out on the hip joint. All showed unmistakable evidence of rheumatoid arthritis on microscopic examination of the synovial membrane. This leads us to believe that degenerative changes, when present, are superimposed on inflammatory changes characteristic of rheumatoid arthritis. In one case, biopsy was performed on the shoulder joint. Likewise in this instance there was synovitis characteristic of rheumatoid arthritis. Our statement of the frequency of involvement of the hip and shoulder joints may not reflect the true incidence of intra-articular involvement in both those regions, but intra-articular involvement does occur in the shoulder, as shown by this example.

The findings reported by Dr. Rosenberg on the incidence of cardiac lesions may be cited in answer to the question asked by Dr. Engleman regarding the incidence of heart disease in cases of rheumatoid spondylitis. Our study did not reveal any unusual incidence of coexisting heart disease in cases of rheumatoid spondylitis. The women in this series did not show any unusual physical characteristics. We encountered all types of body build in both women and men.

We believe involvement of the sacro-iliac joints and the cervical segment of the spinal column may occur without involvement of joints of the thoracic and lumbar segments of the spinal column, in the same way as other combinations of the different regions of the spinal column may be encountered. It is partly because of such distribution that special radiographs to show the apophyseal joints at various levels are often an unsatisfactory adjunct in trying to recognize early evidence of rheumatoid spondylitis in a particular region of the spinal column. There are great degrees of normal irregularities in the structure of apophyseal joints, and attempts to detect abnormal changes in these joints by special radiographs did not seem to us to be helpful in establishing the diagnosis of rheumatoid spondylitis. Either the diagnosis can be made without such special radiographs, or in doubtful cases the special radiographs do not help to establish the diagnosis any more definitely.

The question was raised whether one should regard the finding of bilateral sacro-iliitis as diagnostic evidence of rheumatoid spondylitis. I think one may expect rheumatoid spondylitis to become inactive at various stages in its course, just as peripheral rheumatoid arthritis may " burn out " with varying degrees of residual evidence of the disease. While it may be difficult to be certain in an individual instance, we feel that bilateral sacro-illiitis is rheumatoid spondylitis until it is proved otherwise.

PAPERS FROM BRAZIL

At this point the President said he would like to have read into the record of the meeting the fact that Drs. Marcello and Oswaldo Lucchesi, of São Paulo, Brazil, had contributed to the meeting three papers on the true significance of subcutaneous nodules in rheumatoid arthritis, but that unfortunately the authors could not be present to read them. [An abridgment of the papers in question will be published in the next issue of the *Annals of the Rheumatic Diseases.* EDITOR.]

INCREASED PROTEIN CONTENT OF THE CEREBROSPINAL FLUID IN RHEUMATOID SPONDYLITIS

EDWARD W. BOLAND, NATHAN E. HEADLEY, and PHILIP S. HENCH

The cerebrospinal fluid was studied in fifty soldiers with rheumatoid spondylitis, in thirty-three with spondylitis alone, and in seventeen whose spondylitis was associated with rheumatoid arthritis of peripheral joints. Initial manometric pressures, cell counts, and concentrations of sugar in the cerebrospinal fluid were normal, and the colloidal gold reaction was abnormal in only one case. But there was an increase in the total protein content of lumbar fluid in twenty-one (42%) of the fifty cases. Such increases, when present, were moderate in amount and varied between 47 and 98 mg. per 100 c.cm. The increase in protein of the spinal fluid seemed to be related to the severity of the disease: thus the total proteins were increased about twice as often, and their average concentration was almost twice as high, in the severe, rapidly progressive cases than in the less severe cases of rheumatoid spondylitis. The protein content bore no consistent relationship to the duration of the disease or to the degree of spinal extension, and, contrary to the report of others, it was not increased more often in cases of spondylitis with sciatica than in those without sciatica. Although the spinal fluid protein might be increased in patients with rheumatoid arthritis of peripheral joints, it was increased more often in patients with rheumatoid spondylitis alone, and most often in patients with rheumatoid arthritis of both spinal and peripheral joints.

DISCUSSION

DR. CHARLES SHORT (Boston): Dr. Ludwig, Dr. Bauer, and I started this work in 1935, in the hope that we might demonstrate involvement of the central nervous system in rheumatoid arthritis. Since then pathological studies have shown us that the peripheral nervous system may be involved in rheumatoid arthritis, and Dr. Morrison in our laboratory has found suggestive evidence of changes in the spinal cord as well. That work is still in progress. It still has to be considered as an explanation that the increased protein in the spinal fluid in patients with rheumatoid arthritis actually does reflect changes in the spinal cord or other parts of the central nervous system. Otherwise I do not think we can offer any other explanations than the ones Dr. Boland mentioned.

There are a few isolated points that were brought out in the course of our study. For example, we had three patients with increased globulin in the blood, and all three of them showed increased protein in the spinal fluid. Also, we did combined cisternal and lumbar determinations in several patients, and in one patient a dorsal puncture. Although they all showed a slight increase in the cisternal protein, there was a distinct gradation down the line, and not as much increase in the cistern as one might expect, or as is seen, for instance, in a metabolic disease like myxoedema, where the spinal fluid protein is increased. We were inclined to think that inflammatory changes going on in and around the joints adjacent to the meninges were responsible for the increased diffusion of protein into the cerebrospinal fluid.

DR. EDWARD W. BOLAND (closing): Dr. Short evidently considers differences in the protein content of the cerebrospinal fluid at various levels of the spine to be more significant than we have. It is our understanding that normally the concentration of protein is greater in lumbar fluid than in cisternal fluid. Furthermore, when the cerebrospinal fluid protein is increased as the result of some general disease, such as in myxoedema, the increase is found to be greater in the lumbar fluid than in fluid taken at higher levels. Hence, the fact that the content of protein is greater in the lumbar fluid than in the cisternal fluid in patients with spondylitis does not necessarily indicate that this relatively greater increase is due to local lumbar arthritis and meningeal inflammation; the increased proteins may have their origin at the choroid plexus and, as under normal conditions, may just be relatively more concentrated in the lumbar fluid.

VITAMIN C AND P IN RHEUMATIC FEVER

JAMES F. RINEHART

San Francisco

This paper, briefly reviewing the evidence implicating a nutritional factor in the pathogenesis of rheumatic fever, has already been published in the *Annals*,[1] and, therefore, only a brief summary will be given here. The clinical experiment of Glazebrook and Thomson[2] is cited in support of the concept set forth by the author, that vitamin C deficiency may prepare the soil for rheumatic fever, which is precipitated by infection with beta haemolytic streptococcus. In a group of subjects on a diet nearly devoid of vitamin C all cases of rheumatic fever complicating respiratory infections occurred among those not receiving vitamin C supplements. While vitamin C deficiency may be important in predisposing to the initial attack of rheumatic fever and may be of some value in therapy (reducing incidence and severity of haemorrhagic manifestations), it has failed to exert a curative influence or to prevent recurrences. It was natural to study the influence of vitamin P, a plant pigment which is believed by Szent-Györgi to act in conjunction with vitamin C and exert an influence on capillary permeability. Preliminary observations have strongly suggested that the material does possess therapeutic value. Further study, however, is indicated.

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[1] *Annals of the Rheumatic Diseases*, 1945, 5, 11.
[2] *J. Hyg., Camb.*, 1942, 42, 1.

DISCUSSION

DR. MILTON BORMAN (Milwaukee): What studies were made, if any, on salt metabolism in the treatments, with both vitamin C and P?

DR. CLARENCE L. ROBBINS (New Haven, Connecticut): Was salicylate therapy withheld during this treatment?

DR. RINEHART (closing): No studies were made on salt metabolism although they would perhaps be pertinent. With respect to the use of salicylates, vitamin P was given in addition to the standard therapy the individual was receiving. In San Francisco I think we do not use salicylates quite as liberally as in other parts of the country. A very small proportion of these cases received what we would call large doses of salicylates. For the most part they received the smaller dosage. As far as I know, vitamin P does not itself have a salicylate-like effect.

CHRYSOTHERAPY IN RHEUMATOID ARTHRITIS

CHARLES RAGAN and T. LLOYD TYSON

The use of gold compounds in rheumatoid arthritis is now well established, but reports on the efficacy of gold have been concerned with the immediate response to therapy. In this paper, the results of chrysotherapy after at least a three-year follow-up were presented. The subjects were well-documented patients with rheumatoid arthritis, and the diagnosis was based on the usual clinical and laboratory data, including radiographs, sedimentation rate, and agglutination with Group A haemolytic streptococci. The patients were treated in 1939, 1940, 1941, and half of 1942. The follow-up study was made in the fall of 1945. Patients who were unable to tolerate less than 0·5 g. of gold compound were not included. One hundred and fifty-two patients were treated during the period, and adequate follow-up data were available for 142. The group seemed to be a representative one. The immediate response to treatment was of a type which is generally accepted; 11% showed no improvement, and 50% showed objective evidence of marked improvement. Significant toxicity and response to therapy were similar in the three types of gold used—myocrisin, calcium aurothiomalate, and Solganal B Oleosum. Significant toxic reactions occurred more frequently in patients who had had symptoms for a long time before gold therapy than in patients treated early in the disease. The long-term response to chrysotherapy showed that only 13% of the whole group had not relapsed after three years, while 75% did relapse. The patients showing marked improvement tended to relapse after a slightly longer interval than the patients showing slight improvement. Only 6% could be classified as five-year cures. In general, one should expect a relapse in a patient with rheumatoid arthritis who has had a remission with gold. The relapse was not as severe as the original disease, and of those who relapsed 80% improved on subsequent chrysotherapy. Using this data, we now treat patients with rheumatoid arthritis with a maintenance dose of gold, continuing 50 mg. every two to three weeks indefinitely. In a small group of patients with

psoriasis accompanying the rheumatoid arthritis the response to gold was less satisfactory than in the group as a whole. The mechanism of the action of gold in rheumatoid arthritis is not known, but it is suggested that the gold acts as an enzyme inhibitor, and, when excreted, the process becomes reactivated and a relapse occurs.

Discussion

Dr. Smith (Philadelphia): On the original administration of gold, was it given in courses with rest periods in between or in continuous dosage? Were toxic effects more apt to occur after a rest period, or when gold was given in another course?

Dr. Richard H. Freyberg (New York): This is the first American report I know of which reviews a large series of cases observed over a sufficient period to reveal more than the " early results " of gold therapy. There are three limitations to the use of gold as a therapeutic agent. First, not all patients who have rheumatoid arthritis in an active stage respond favourably. Secondly, toxicity is always a potentiality. Thirdly, relapse or exacerbation may occur after benefit from earlier gold therapy. We have heard to-day that the rate of relapse or exacerbation is very high. The longer I observe patients treated with gold, the more I am impressed that many who improved during and after the use of gold, grew worse after therapy was stopped. This led us to use sustained treatment. We have not yet had the opportunity to observe long enough to be certain of the benefit, but our impression is that there are fewer and less severe relapses when treatment is sustained. It would appear that a certain amount of gold is required to sustain the arrest.

In the experience of the authors, was toxicity frequent or severe if it occurred during treatment with a sustaining amount of gold? If there was little or no toxicity, during more intensive treatment which was later lessened, what was the incidence of toxicity?

It is my impression that, if courses of treatment are used, with second or third courses given to patients who benefited from an earlier one, the degree of improvement and the reduction in sedimentation rate were less with subsequent treatment. For example, some patients had what appeared to be complete arrest; treatment was stopped and after several months or a year the arthritis would recur. Treatment with gold at this time was often less helpful than previously.

It should be emphasized that gold therapy, like all other single measures, is certainly not a complete treatment: if it has value, it should be used along with a good general programme.

Dr. Otto Steinbrocker (New York): An interesting presentation has just been given, but I cannot quietly accept the opening statement that the use of gold is well established. It can only be said that it is well established in the minds of those who think that gold is a good therapeutic measure in rheumatoid arthritis. There are those of another mind, I believe, on the subject. I do not mean to disparage what has been done. Therapeutic study, and any effort to treat these patients effectively, is a worthwhile activity. I do think we must exercise certain precautions in evaluating results. Gold has been used eighteen years. Yet it is still difficult, after going over much of the literature, to decide just where to place it as a therapeutic measure in the treatment of rheumatoid arthritis.

How many of these cases were early? That is an essential index to what happens in therapy. In our survey of the literature we have made a chart of the results of chrysotherapy. Those who got the best results treated the most early cases.

On the matter of subjective effects, isn't it a rather misleading criterion to use? When a drug is on trial (and as far as I am concerned, this applies to gold as a therapeutic agent) I don't believe we should be guided by any but objective responses in arriving at its effectiveness. Then, what does " improvement " mean? Standards of improvement are quite different. In reading the literature you are bound to be amazed at the diversity of what some people consider improvement and what others require before they will classify the patient as improved.

I would like to call attention to the fact that 9% of cases were arrested. In a series we followed for one to five years we observed an even greater number of arrests, probably twice as many. It was a much smaller series; there were only forty-three patients we were able to follow that long. The amount of improvement was very small, and it did continue. But the total figures would agree with Dr. Cecil's, and with what the original study of Dr. Boots and Dr. Dawson showed. The basic figure here seems to be great improvement (and that is the only degree that deserves any respect with a drug on trial) or arrest in 40 to 50% at the end of a reasonable period of follow-up. The Harvard group has found that without chrysotherapy they can duplicate those figures. When dealing with a toxic agent we should be careful about attributing too much value to the drug unless it is definite. I think the only conclusion we can draw, in view of the low number of arrested cases, is that at best there is some palliative effect.

DR. H. M. MARGOLIS (Pittsburgh): I have been impressed with the fact that the more we use gold, the larger our experience, the more questions we develop that we cannot answer very well with regard to toxicity and the variable therapeutic results. A disconcerting experience is a relapse developing in certain patients treated with gold some time after practically complete arrest of activity of the rheumatoid process. I don't know exactly what our incidence of such relapses is, but it is much higher than we should like it to be.

Contrary to the experience reported in this paper, we have found that, once a patient has developed a relapse, the result of a repetitive course of gold therapy is rarely as good as it was the first time, even though the patient responded well to the first course of therapy. In some of our patients whose disease was practically completely inactivated and remained so for a period of time, we were sometimes unable to obtain any significant clinical improvement with further gold therapy given during the relapse. In fact, some of these patients get progressively worse despite the administration of a second course of gold. That has taught us that if we get a good result with gold therapy the course of therapy with gold should be repeated after a rest period, which we have gradually shortened to six or eight weeks. We used to allow these patients an interval of three or four months, but we found that to be too long, for most relapses occur after the second or third month. We therefore administer the second course of gold within six to eight weeks after completion of the first course. By so doing, our results have been much better. We have, I am sure, thus prevented relapses in some of our patients, and induced more lasting remissions or arrest of the disease. In a few instances we have tried small sustaining doses of gold, but that procedure was so ineffectual that we discontinued it. Furthermore, we were rather hesitant about continuing the administration of gold to a patient who already had had what we considered an adequate amount.

DR. JOHN W. GRAY (Newark, New Jersey): For a long time I hesitated to use gold, until I finally took a group of cases whose sedimentation rates remained high and who had not improved at all after more conservative treatment for a long period. I was satisfied after a period of observation and treatment that a large number of those cases improved, that I felt justified in continuing the treatment. I have now used it in many cases, but I am disappointed, not in the results obtained but in the large number that cannot continue taking gold; a weekly blood count and urinalysis during gold administration shows that many develop a hyalin cast or neutrophilia, and I immediately stop treatment until the normal level is regained. I also stop if there is any itching or slight rash. This brings up a point which I think is very important, and that is the warning to men who are using gold without an adequate check. The only cases of severe reaction that I have had to treat are those that have been given gold without any tests or observations regarding toxicity. I have had two or three very bad cases of exfoliated dermatitis come to me: one said that his doctor had given him gold for four-and-a-half months twice a week and no tests were ever done. I do not know how we can control that, but it is very serious.

Is there any information regarding the toxic effect of gold on a foetus in a pregnant woman?

DR. ROLAND DAVISON (San Francisco): Has Dr. Ragan evidence that gold acts as an enzyme inhibitor?

DR. RALPH H. BOOTS (New York): I have had the opportunity of observing the work of Drs. Ragan and Tyson. Dr. Ragan emphasized two points: (1) that patients who have had remissions of their disease following gold therapy will have a high percentage of relapses after a period of six months to five years; and (2) that if a physician uses gold therapy it would be advisable after giving the course of gold to continue the patient with maintenance dosages. We can keep on discussing the question of whether or not gold is an excellent therapeutic agent without arriving at a conclusion. Dr. Ragan's opening statement that gold is a well-accepted form of therapy for rheumatoid arthritis is based chiefly upon the fact that there have been so many papers published in favour of it, and very few men who have worked with this form of therapy have given adverse reports.

DR. WALTER BAUER (Boston, Massachusetts): Dr. Ragan's timely report should be of interest to all of us since it indicates that the therapeutic efficacy of chrysotherapy in rheumatoid arthritis remains to be established. It also serves to emphasize the need for long-continued observation of patients with rheumatoid arthritis who have not received any of the so-called specific therapeutic agents.

The latter type of study has been in progress in our clinic since 1928. The first three hundred patients with rheumatoid arthritis admitted to the hospital were studied in detail and have been observed in a special follow-up clinic since then. During this period they received only general therapy. The clinical course of the disease as observed in this group of patients up to 1937 was equally as good if not slightly better than that of the gold-treated patients reported in the literature up to that time. I am sorry a follow-up study of this same group, up to January, 1946, is not available for comparison with Dr. Ragan's report. During the few months I have been back in the clinic I have seen many of the patients from this original series, some of whom are enjoying excellent remissions of years' duration and doing a full day's work. Whether the percentage number exhibiting marked improvement is as great as Dr. Ragan has reported I do not know; I would guess it is.

I am sure we all wish we could predict with some degree of accuracy the course of rheumatoid arthritis in a given patient. Unfortunately these patients do not wear such prognostic labels when they consult us for treatment. If they did, the judging of therapeutic results in rheumatoid arthritis would be a relatively simple matter. We have all seen patients with rheumatoid arthritis who have experienced severe attacks lasting months or years and who have had excellent remissions without the benefit of "specific therapy". If such patients had received gold therapy it would have been extremely difficult, if not impossible, to determine what degree of improvement was the result of treatment and what represented the natural course of the disease. There is little doubt in my mind that natural favourable fluctuations of the disease have often been considered the result of the treatment administered. If such were not the case the same mystical figure of 70% improved would not appear as frequently as it does, irrespective of the type of therapy employed. Of the small series of patients that we have treated with gold salts only 20% have shown good objective evidence of improvement. There are many reasons for doubting the specificity of chrysotherapy in rheumatoid arthritis that has been claimed by some authors. These will be presented elsewhere in the near future. We predict that chrysotherapy will be dropped completely in years to come. We may be wrong; we hope we are.

We shall attempt to make available at an early date* the present status of the three hundred patients who have been under observation since 1928 without the benefit of specific therapy, so that they will be available for comparison with studies such as Dr. Ragan has presented.

DR. R. M. STECHER (Cleveland, Ohio): We have experience in close to 300 patients who were treated with gold for rheumatoid arthritis, and for comparison with our findings I would like to ask a few questions. Which criterion did you use for marked improvement? Which criterion did you use for only slight improvement? Was it the clinical picture? Was it laboratory tests?

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* This study was reported by Drs. Charles Short and Walter Bauer at the June, 1947, meeting of the American Rheumatism Association.—*Ed.*

Was it sedimentation rate only? Was it the blood count? Was it the change in the agglutination for Group A?

We do not base our judgment any more only on the change of sedimentation rate. We do not treat the patients for sedimentation rate; we treat them for the condition. That is why we go definitely by the clinical improvement and by more than first changes of the sedimentation rate. We know there could be a good improvement without a change of the sedimentation rate. The reason is not up for to-day's discussion.

Do you know any contributing factors for the toxicity of gold? We think we have found some. We do not think that it is just gold, no matter what you are using. Some of our patients who had a heavy metal rash on the skin got it mostly on those parts that were exposed to sunlight, so we think maybe the gold isn't so toxic in itself; maybe it does something to help the effect, for instance, of sunlight, to come out in such a bad effect.

When did you stop the gold injections? Did you believe in a total dose? If so, what was the average dose? We have tried to build up the dose to the first which shows improvement, and we call that the optimal dose. We have reason for this, because very often when we were still increasing the dose, expecting we could do something extra for the patient, we got some local reaction in the form of more pain or swelling.

At the beginning of our treatments we thought we had to stop after administering a certain amount of gold, not only because we were satisfied with the improvement, but because we were afraid of the toxic effect if we exceeded a certain total dose. We do not do that any more, because we think it is better to keep the patient to a maintenance dose, a very small amount, and not allow him to stay away from treatment three or four months as is done so often.

DR. GORDON BUTTORFF (Louisville, Kentucky): I became interested in rheumatism about five years ago because no one in Louisville was doing much about it. I was interested in using gold, and the first thing I knew I was getting most of the cases of rheumatoid arthritis dumped in my lap. The other men were treating them with conservative methods such as have been outlined. Dr. Freyberg has mentioned that in using gold therapy we should use all the other adjuncts to therapy that we know about. Gold should be used in addition to these other methods, and I think in the hands of those who watch their cases closely it is not too dangerous. Certainly if I had rheumatoid arthritis, after some degree of experience with it, I would be inclined to want gold therapy myself. I think that probably is a question we should ask ourselves: would we use it on ourselves or on our own families? So often those who are opposed to gold use it as a last resort. Also many of the men who use it admit that they have used it in a very small percentage of cases; while others have not had the opportunity to follow their cases for any length of time. I have thus far not heard any individual who has had any great experience with gold say that he has stopped using it and has gone back to other forms of therapy.

Our experience has been like that of several discussants; we find it is more difficult to get improvement after a patient has had a remission. Another point is that some of the patients in whom you have to stop gold therapy because of dermatitis or pruritis (we stop it temporarily with pruritis) have a temporary lay-off and can be given gold therapy successfully again.

I think that the best results are gotten with gold therapy if you use it early. You may ask, " How do you know they wouldn't get better, anyhow? " We don't, but if we use it along with these other therapeutic measures, then I think we have an additional therapeutic measure to help these patients.

DR. DAVID HIRSCH KLING (Los Angeles): Our experience in over five hundred cases treated with gold for ten years coincide with the authors' experience. We perhaps have not seen as many relapses, but this may be accidental. I am very much against the trend in recent papers, which state that gold is still on trial. Even the first significant papers on chrysotherapy published in the United States have stressed the frequency of failures, relapses, and the danger of toxic reactions. It was repeatedly declared that gold is not the ideal therapy for rheumatoid arthritis. In this sense almost every therapy is on trial. We always thought that the arsenicals in syphilis

approached the standard of a specific therapy; but suddenly everybody turned away from them to penicillin. The arsenicals were not so good after all. Toxic reactions were not reported so extensively as with gold therapy. Not every transitory rash, every scratch, was reported. And, of course, in five hundred patients with rheumatoid arthritis scratches and rashes do occur, even if they do not get gold. I have to say this for Dr. Cecil, Dr. Dawson, and Dr. Boots, and for all who used gold when lots of people were against it; they took a real chance and they had a good experimental and clinical background. I like Dr. Bauer's attitude. He says, " It is not good, we don't use gold ". But I don't like the statements in recent papers: " We use gold, but under strictly controlled methods, because half the patients get only saline, or oil, and the other half get gold." One author just hit the bottom; he is blindfolded, he does not know to whom he gave gold, to whom he gave oil. Such methods are all right for laboratory experiments, where one selects one strain of rats and inoculates them at one time with equal amounts of one microbe. Their uncritical application to clinical medicine, especially to such a complicated entity as rheumatoid arthritis, is apt to be misleading. We prefer clinical controls and judgment. I would like to point out to Dr. Steinbrocker that even ten years ago the American publications on gold therapy regarded only remissions and marked improvement as significant successes, although they listed the percentages of slight improvement. Dr. Cecil gave the duration of remissions up to five years and the percentage of recurrences.

I am very grateful for this fine paper.

Dr. Douglas Taylor (Toronto): It might be well to draw the attention of this Society to conditions faced by the general practitioner. They are the ones who first see the patients with arthritis, and treatment is carried out by whatever means available and compatible with a busy practice. Injection methods seem favoured because they are time-savers. Many practitioners now are tempted to use gold as an easy method for treating " arthritis ", but many seem to forget that gold may cause serious complications. It is suggested that writers of articles favouring gold therapy in rheumatoid arthritis should emphasize the need for careful repeated examinations to try and prevent the development of complications. Any therapy that has a mortality rate should be used with great caution, especially while it is in the experimental stage.

Dr. Russell L. Cecil (New York): I have seen some of the most satisfactory results marred by too early return to work. If you take the well-to-do patients in private practice, they can stop work and give up their routine life maybe for a year or so, and obtain enough rest to desensitize the joint tissue; whereas if you let the young man or woman who has to work hard for a living go back to work and stand all day over some difficult job, or go back to a factory, or back to nursing three or four children or running a house or going to market every day, the environment for permanent recovery is not established. The minute you put that patient back into the routine of life and into the struggle for existence he does not need a psychic shock; the mere routine of his life invites a relapse. I do not know how we are going to solve this problem, because the working classes do have to go back to work much sooner than they should. I have been distressed time and time again to see a patient who had done beautifully in the clinic go into a relapse after three or four months of routine work. So if I had my way I would not let any patient with rheumatoid arthritis go back to work for maybe a year after they had had a remission. That ties up with what Dr. Bauer had to say, because I am quite sure that rest in bed and institutional care, such as Dr. Bauer gives his patients, are ideal for the arthritic patient; but it is just impossible and impractical at the present time to put these ambulant patients into institutions and to give them the proper rest in bed.

I think that in febrile cases it is well to have a combination of rest in bed, institutional care, physiotherapy, transfusions, etc., combined with gold. If this is not the ideal treatment, certainly it is the best treatment we can give those patients at present.

I am glad to hear the emphasis on early cases. I think that there we have a reversible process; and, whether we use rest in bed or gold therapy or the climate cure, they are the cases that are really amenable to permanent cure.

I hope we shall not have any more advocates of gold therapy after " everything else has been tried ". That is a very malicious doctrine. I believe that we are all interested in this " maintenance dose " of gold therapy. We have not worked it out yet, but it seems a more logical way of using gold than the " course " method originally devised by European writers.

This has been an interesting and profitable discussion, but we must all admit that we are still suspended in air. Though it is a rather terrifying prospect, someone has got to buckle down to this gold problem and give us a ten-year follow-up study of cases treated with and without gold. That is the only way ever to answer this question finally.

DR. CHARLES A. RAGAN (closing): Dr. Smith asked about the courses with rest periods between. When we started using myocrisin, in 1939, quite a few patients received 2 and 3 g. of gold with a month in between each gramme. There was no difference we could figure out between the relapses in those people who got 3 g. and those who got 1 g. The figures are not enough to make a statistical analysis. In relation to the toxic effect after a rest period, I think he is implying there is some sensitivity and you sensitize the patient. We cannot see anything in that respect. Toxicity develops at any time during the course of therapy, and there is no increase in incidence immediately following resumption of therapy after a rest period. I would not hesitate to subscribe to everything that has been said about toxicity. We are in a continual state of alarm in giving this drug.

Dr. Cecil brought up the point that most of Dr. Bauer's patients were resting in bed. Whether we can compare the two types of treatment I do not know, but it is completely unfeasible for us in New York to hospitalize all our patients. In answer to one of Dr. Steinbrocker's questions, there were twenty-one patients out of 142 with a duration of illness of less than one year; but the early patients relapsed at the same rate as the late patients, and we could determine no difference between them as far as duration goes, as to who improved in the second course. The subject of response was not mentioned except to differentiate between whether the 5% have a difference between subjective and objective response. All the other improvements were based on objective criteria.

We are not convinced that sunlight has anything to do with the development of dermatitis. We have tried to produce it in animals by exposing them to ultra-violet radiation, but without success. The average treatment with gold in this series was mentioned as 1,250 mg. Some got 400, some got 500, and so on, but the average was 1,250. About these warning signals by doing laboratory methods—I mean, your blood counts and urine analyses—I know of no way to detect impending dermatitis. We have followed our cases with reasonable care. They still develop dermatitis. There is nothing preceding it that we know of. Some patients develop eosinophilia without subsequent dermatitis, and some develop dermatitis without eosinophilia; but as far as the haemopoietic system is concerned you can foresee it before you get any trouble. I look on this as purely a heavy-metal poison. This applies as well to toxicity to the renal system. If you stop gold, toxicity will usually subside. We had a person with a nephrotic type of picture who suddenly developed albuminuria which persisted for two years.

I don't know anything about pregnant people or the foetal response to gold. Most of our patients, when they get pregnant, have a remission. In answer to Dr. Davison, the enzyme system was a shot in the dark. I have no idea what enzyme it is, so I cannot say.

One objective sign of improvement I think we have is the reversal of the agglutination with the haemolytic streptococcus. In using our technique, which is a little different from Dr. Cecil's, we have not seen more than one agglutination turn from positive to negative, using the conservative treatment when used in a clinic with ambulatory patients. With chrysotherapy, we have seen seventeen. However, I do not think this is the place to go into how we determine cures or how we determine improvements. It would take all week to discuss that. Suffice it to say that these patients showed improvement by being able to go back to work, by loss of pain, by a fall in sedimentation rate, and, in seventeen of them, by reversal of the agglutination with haemolytic streptococci. Everybody has pointed out that in a second course of gold your improvement is

not as marked as on your first. There are a lot of factors entering into it, including the factor that the patient is very sick when he first comes in. He relapses before he gets very sick again. How to evaluate how much improvement you get is something I do not know. We feel the course method of treatment of gold is not the answer to the problem any more than that gold is the answer to the problem of rheumatoid arthritis; but we feel that perhaps we can prevent these relapses by sustaining doses of gold.

PROLONGED ORAL ADMINISTRATION OF PENICILLIN IN RHEUMATOID ARTHRITIS

JAMES A. COSS, JR., RALPH H. BOOTS, and MIRIAM OLMSTEAD LIPMAN

New York

A study was made of the effect of penicillin given orally, over periods up to six months, to ten arthritic patients. It was felt that early studies of the effect of penicillin on rheumatoid arthritis had been incomplete and inconclusive for two reasons: (1) because the dosage of penicillin used had been quite small, and (2) because penicillin had been administered for only a short period of time. Among various suggested aetiologies, it had been proposed that rheumatoid arthritis was a result, not of any one attack by micro-organisms, but of a series of insults which finally culminated in a reaction by the body. For this reason these workers had made a study of the results of therapy in a small group of patients who had been treated with oral penicillin for periods of from two to six months. A careful study had been made of the bacteriological changes, penicillin blood levels, appearance of sensitivity, and appearance of resistant micro-organisms.

Experimental.—Two cases of juvenile rheumatoid arthritis, two cases of Marie Strümpell spondylitis, and six cases of adult rheumatoid arthritis were chosen for this study. The Marie Strümpell cases and the six adult rheumatoid arthritis patients had been previously untreated but had clinical manifestations of moderate to marked arthritis, and all of the six adult patients with rheumatoid arthritis had a positive streptococcus agglutination. No previous treatment had been administered, and during the course of this study they were given no treatment other than aspirin with their penicillin.

Dosage Schedules.—All adult patients received 1,000,000 units of penicillin daily in six divided doses. The two children in the study received 500,000 units of penicillin daily. This was given without any buffering agent or other means of combating gastric acidity, and the penicillin was simply mixed with tap water before ingestion.

Clinical Results.—The effect on the arthritis was indifferent.

Penicillin Levels.—It was found that from two to four times as much oral penicillin had to be administered to obtain levels comparable to those obtained with intramuscular administration. Non-buffered penicillin apparently gave levels as satisfactory as penicillin in oil or with various buffers. Thus far there had been no instances of toxicity or sensitive reactions.

Bacteriological Results.—Striking findings had been the appearance of coliform organisms in the oropharynx and, in the majority of instances, of a brown discoloration of the tongue, which was tentatively identified as a fungus. Changes in the intestinal flora, though less striking, were definite. Non-haemolytic streptococci, recovered from most of the stool specimens before penicillin, were found only infrequently during treatment.

The relationship of the concentration of penicillin in the serum to the sensitivity of the organisms isolated was determined.

Discussion

Dr. Philip Lewin (Chicago): I know of a patient who is taking penicillin by mouth for sinus trouble, and has improved. She had brown and black discoloration of her tongue and teeth, which disappeared when she discontinued using a dentifrice that contained perborate. It may be of interest to know that very shortly the brown colour is going to be taken out of penicillin.

Dr. H. M. Margolis (Pittsburg, Pennsylvania): It might be of interest to relate briefly our experience with eleven patients with active rheumatoid arthritis treated with large doses of penicillin. We started our work just about the time Dr. Hench's report appeared. The first patient received 400,000 units daily for four weeks. The other ten patients, treated after Dr. Hench's report was published, were given 800,000 to 1,000,000 units daily for a period of four to six weeks. We administered these large doses of penicillin for such long periods in order to be sure that any failures in therapeutic results might not be attributable to inadequate dosage. The only patient who showed slight improvement, for but a short period of time, was a girl who received the 400,000 units daily. All the other patients showed no effect whatsoever from the administration of penicillin. Our conclusion, therefore, was that penicillin given in the dosage used was ineffectual in rheumatoid arthritis.

Dr. James A. Coss, Jr. (closing): We have received a small amount of colourless, or crystalline penicillin, which we are planning to use to see what might occur.

Dr. Barach at our institution has been using penicillin aerosol for some time, and has noticed the appearance of a brown tongue, just as we have. He recently has begun a study with aerosol penicillin using crystalline material to find out if the colour is due to impurities of the older material. If the colour were to disappear during administration of crystalline penicillin, that would suggest that the coloration of the tongue is due to a concentration of impurity in the yellow penicillin.

DEGENERATIVE BONE DISEASE

WALTER M. SOLOMON
Cleveland, Ohio

Dr. Solomon was unfortunately unable to be present to read his paper on the findings in eighteen patients with posterior spurs of lumbar vertebrae ; but its title was recorded.

THE EFFECT OF PROSTIGMIN (NEOSTIGMIN) ON THE MUSCLE SPASM OF RHEUMATOID ARTHRITIS

VICTOR G. BALBONI, JOSEPH L. HOLLANDER, and DAVID M. KYDD
From the Rheumatic Disease Section, Ashburn General Hospital

Prostigmin has been advocated in recent years for the relief of muscle spasm in anterior poliomyelitis and in a variety of diseased states of the central nervous system. More recent work has suggested that prostigmin might be of value for the relief of muscle spasm associated with arthritic conditions. Prostigmin in doses up to the limit of tolerance was, therefore, administered to twenty-three patients with rheumatoid arthritis in an attempt to relieve the associated muscle spasm. In no case was a satisfactory therapeutic response obtained. Only two cases showed any appreciable decrease in muscle spasm, and even in one of these the effect was inconsistent, as the spasm about other affected joints coincidentally increased. The second case had already started into spontaneous remission. Prostigmin caused unpleasant and often alarming reactions in fourteen of the twenty-three cases studied. These workers, therefore, were unable to recommend prostigmin in the treatment of rheumatoid arthritis.

Discussion

Dr. Ralph Pemberton (Philadelphia, Pennsylvania): Some five years ago Dr. Scull, Dr. Persani, and I, animated obviously by the same reasoning which led Dr. Cohen and his associates to take up this problem, attempted to influence the conditions of the joints in the arthritic by means of prostigmin. Our efforts were not so thoroughly conducted, probably, and certainly the cases were not as numerous, but in general we did not feel encouraged to go on, and, therefore, it came as rather a surprise to us to find that a more serious and sustained attempt was alleged to have had successful results.

Dr. Philip Lewin (Chicago): I consider this a very important paper. When so many of our patients get their medical information from lay magazines, and when some of the editors and the writers of these articles earn their living by publishing things that they hope will be proved by medical investigation—but many never will be—it is high time for us to tell the people that they had better get their information from their general practitioner, and if he does not know, from his buddy who is an expert or a specialist. There was a time, soon after I came out of

service, when I had six or eight calls a day to the effect: " Do you think prostigmin will help me? I read about it in such and such a magazine." I think that is a serious situation.

About the infantile paralysis part of it, after Kabat and Knapp had written their article in the *Journal of the American Medical Association* (1943, **122**, 989), a large series of cases was treated at Michael Reese Hospital in Chicago; no data were obtained that would sustain the statements made regarding poliomyelitis. If you knew what is behind some of the controversy regarding spasm in poliomyelitis, you might understand why one group is trying to prove what has been said and another group trying to disprove the same thing.

About the goniometer, I think there ought to be a short course in medical schools teaching students how to measure joint movements. I venture to say that if a patient were before us at this moment and twenty of us, with the finest goniometer, were to measure his joint movements, we should get some variable results.

DR. ABRAHAM S. GORDON (Brooklyn, N.Y.): We were intrigued by this drug, prostigmin, a number of years ago, and had the opportunity to study it four years before this whole commotion about the effect of prostigmin in rheumatoid arthritis. The company that gave us the supply of the drug was very much interested in a favourable report, and when we could not give them such a report, they took their business somewhere else and got a favourable report from someone in Philadelphia. This prostigmin is a fascinating drug, both pharmacologically and clinically. It has peculiar side-reactions which were not mentioned. Some patients are very sensitive to it and feel sick after receiving it. The symptoms of nausea, cramps, dizziness, and fainting spells are not uncommon. Patients must be asked to stay in the office fifteen, twenty, or twenty-five minutes before leaving. I have heard of calls from the outside, from a druggist or a doctor, saying that the patient had an injection recently and fell in the subway or in the street car and fainted. Such incidents are not pleasant.

In addition to this question of muscle spasm, prostigmin does have an effect on the peripheral vascular bed which has not been mentioned. We hope we will be able to make it the subject of a future report. We have studied this drug in approximately one hundred patients in the clinic over a period of four years. There are definite changes in certain types of peripheral circulation. Some are good and some are not so good. Generally, in the relief of muscle spasm it has not been as effective as it was claimed to be, and the more one uses the drug on a patient the less effect it has.

DR. OVIDIO MIQUEL (Asuncion, Paraguay; at present Research Fellow in Pharmacology at Cornell University Medical College, New York City): At the Department of Pharmacology, Cornell University Medical College, a group of investigators attempted to explain further the mechanism of action of prostigmin and physostigmin. Part of this work was reported in Atlantic City last March, at the meeting of the American Federation of Biologic Societies. The papers will be published in the *Journal of Pharmacology and Experimental Therapeutics* in the summer or fall of this year.

It has been generally stated that prostigmin exerts its pharmacological action by its ability to inhibit an enzyme known under the name of cholinesterase. Riker and Wescoe in our Department used the cat soleus-gastrocnemius preparation, with the sciatic nerve sectioned and the popliteal artery dissected for intra-arterial injections. They showed that prostigmin acts directly upon the skeletal muscle in which cholinesterase has been destroyed by a potent anticholinesterase agent, di-iso-propyl fluorophosphate. Riker and Wescoe's procedure was as follows: they injected 25 gammas of prostigmin per kg. intra-arterially in cats in which the cholinesterase of the muscle was completely inactivated, and obtained typical contractile responses.

To eliminate the possibility that endogenous acetylcholine may play a rôle in those responses, the experiments were repeated in cats seven to eleven days after the section of the sciatic nerve, since it is known that after that period there is no acetylcholine present in the nerve ending. The results showed that prostigmin acts on chronically denervated muscle, and demonstrated that prostigmin is able to provoke muscle contraction in absence of cholinesterase and acetylcholine.

I worked with the frog rectus abdominis muscle preparation and was also able to show that prostigmin provokes muscle contraction in the absence of cholinesterase. In conclusion I might add that in these experiments prostigmin produced contraction and not relaxation of the muscle.

All the experiments were carried out on normal muscles. As far as I know it is difficult or impossible to produce muscle spasm in laboratory animals, except by means of a specific dietary insufficiency, which is under study by a group of investigators in this city.

DR. CORNELIUS H. TRAEGAR (New York): We are in the throes of conducting a follow-up on patients with rheumatoid arthritis and spondylitis who have been treated with prostigmin since 1934. To date we have exactly twice as many patients as were reported by Dr. Balboni, and my offhand comment is that our results are exactly as those reported by him. Our supply of prostigmin has been cut off for the same reason as was previously mentioned.

DR. PHILIP S. HENCH (Rochester, Minnesota): Dr. Balboni and his associates have done a service to the members of this Association, many of whom have been flooded with requests from patients for information regarding the effects of prostigmin for rheumatoid arthritis. As we have heard here to-day, several American rheumatologists have studied for many months, even years, the effects of this remedy but have not published their results because the latter were unimpressive. Hence we have heretofore not had much information to give to our patients. With the publication of the reports and remarks made here to-day, physicians and patients will be better informed and need not rely only on certain undisciplined writings which have appeared in the popular press. We may be annoyed by these writings, but we must not be annoyed at Drs. Cohen and Trommer either because we cannot agree with their evaluation of prostigmin or because, unfortunately for them, their work was ballyhoed by a non-medical writer. Drs. Cohen and Trommer have a perfect right to their opinion and to their enthusiasm. They even have a right to be wrong. Haven't we all thought too highly of some remedy that was later discarded?

Will Dr. Freyberg tell us of his unpublished results with prostigmin and allied substances? Will Dr. Trommer tell us his present views on this subject? Will Dr. Balboni tell us if he has found physostigmin to be any better than prostigmin?

DR. RICHARD H. FREYBERG (New York): Dr. Traeger reported that our clinic's results are comparable to those of Dr. Balboni. Independent observations of mine are similar. I told Dr. Hench in personal conversation that recently I have been using prostigmin chiefly to demonstrate to those patients who "insist" upon having it that it does not have the benefit claimed for it.

DR. CHARLEY J. SMYTH (Eloise, Michigan): We, too, were deluged by the same requests from patients in our area. We were more or less forced to try to obtain some data on the point, because there were not sufficient facts available to pass adequate judgment. We treated, in Wayne County General Hospital, about twenty patients with this material, according to the technique that the previous authors had recommended. We tried to obtain the element of control by treating these patients with the material advocated for a week or ten days, then substituting saline control after discontinuing the physostigmin and giving them only atropine. Our results are entirely in accord with those of Dr. Traeger, Dr. Freyberg, and the others. We were not at all impressed. Subjectively many of the twenty patients had just as much improvement with the saline control as they had with the physostigmin and atropine.

DR. EMANUEL (New York): Before we discard prostigmin completely we should dwell a few moments on its action on the vascular bed. The drug is undoubtedly powerful in this regard. For example, in the pelvis it creates a massive hyperaemia great enough to bring on delayed menstruation. That action has been substantiated by eight or nine different reports in the literature. If this can occur in the visceral organs, it can occur possibly in the peripheral vascular bed, so that our emphasis upon the neuro-junction is probably less important than our emphasis upon the vasomotor dilatation which may occur in places where such effects may be beneficial. Before discarding it completely we should bear in mind that further vasomotor action of prostigmin should be considered.

DR. TROMMER (Philadelphia, Pennsylvania): The intrathecal injection of neostigmin was

shown by Cramer and other investigators to inhibit some hyperactive reflex in conditions such as hemiplegia. Schweitzer and Wright (this is from Kabat's paper), demonstrated in animal experiments, that neostigmin, acting directly on the spinal cord, had an inhibitory effect on the knee and could restrict motion. It probably acts centrally; exactly where is not known.

An interesting statement is made by Ward and Kenard that monkeys rendered hemiplegic by excision of the motor cortex recovered motor function more rapidly when given a cholinergic drug. This is an astounding statement. In speaking on this subject at the American Physiotherapy Congress in Washington several weeks ago, Dr. Erlich quoted from a list of about seventeen references. He also was very much impressed at the time with the fact, the reason of which was not known to him, that a more rapid regeneration occurred when a cholinergic drug was used.

As to the paper presented by Drs. Balboni and Hollander, we followed through with Dr. Kabat's recommendations in poliomyelitis, by giving prostigmin by mouth. Since then we have discarded this method. We found little if any efficacious results with the administration of prostigmin orally in rheumatoid arthritis.

In the acute case it is questionable whether prostigmin, or the natural drug, physostigmin, will be able to exert a sufficient neutralizing action resulting in an antispasmodic effect.

The type of case which appears to respond favourably is not one which receives a single injection but one which receives a series of injections. Physiotherapy, such as active exercise, can help to initiate increased motion. The type of rheumatoid arthritis where inflammation in the joint has subsided and there is evident muscle spasm is the type we have described. This type of case results in permanent deformities; it may respond and has, in a certain number of cases under my personal supervision, with the use of prostigmin or physostigmin hypodermically. This will not affect the progress of the disease, but will relax the muscle spasm which is causing deformities and limitation of motion.

I have been interested in muscle spasm regardless of the origin. In the cases in which the tremor is due to Parkinsonism, I have not found any effect whatsoever. In certain cases of poliomyelitis (I say " certain cases " advisedly), where the muscle spasm is present without contracture or fibrosis, both of which are irreversible processes, an effect may be had by using prostigmin or physostigmin. Relief of muscle spasm by cholinergic therapy over a period of time increases motion and restores partial function to an extremity. This effect can be further enhanced by the use of concomitant physiotherapy.

At present there is controversy as to what muscle spasm actually is in poliomyelitis. It is important for physicians to recognize the existence of muscle spasm in chronic arthritis. I would like to cite a case of Little's disease presenting marked athetoid movements and scissor gait. The patient appears to be thirteen years old but is actually thirty-two years of age. After a six months' trial period of therapy, no response was had except that the patient said she would like to continue because she felt somewhat different. On that basis I continued to give her injections of physostigmin plus atropine three times a week. At the present time the patient is able to spread her legs, the scissor gait has decreased so that her toes are spread out and are less indented, and the athetoid movements have improved to such an extent that a dentist can now work on her teeth.

This is an isolated case. There are probably certain types of cases where the involvement has a neurological component. I cannot quote directly, but reports have been appearing in the literature where encouraging results have been obtained in these spastic types of cases. Clinically it is very difficult to make a sharp distinction between muscle spasm and permanent deformity. I don't think it has as yet been made even by the electromyograph. If lengthening of the shortened muscle occurs by therapy, then that muscle was not in absolutely irreversible contracture or fibrosis. If any mode of therapy, whether manual or otherwise, produces muscle lengthening, then it is in the end-results that you see the distinction rather than in the clinical observation. Clinically, however, one can often feel a spastic hamstring muscle and with gradual pull can

increase length and range of motion. When this is the case one can assume that a spastic muscle exists.

Prostigmin is only an adjunct as far as treatment is concerned. The effect by mouth is practically nil. It should be given by hypodermic injection daily over a reasonable period of time. Drs. Balboni, Hollander, and Kydd state that they gave one hypodermic injection of 1 c.cm. 1 : 2,000 prostigmin bromide, 15 mg. three times a day orally. This does not comply with the procedure as set forth in our original paper. We gave hypodermic injections at least three times weekly along with the oral medication. Incidentally, we now sometimes administer physostigmin salicylate two or even three times daily and use no oral medication.

DR. VICTOR G. BALBONI (closing): We have had no experience with physostigmin, but would not expect that it would be more effective.

THE EFFECT OF RÖNTGEN THERAPY IN RHEUMATOID SPONDYLITIS

RICHARD T. SMITH, EDWARD W. BOLAND, and PHILIP S. HENCH

Army and Navy General Hospital, Hot Springs, Arkansas

Seventy-five patients with proven symptomatic spondylitis were studied by these authors for six months. Twenty-five received röntgen therapy only for five months; twenty-five patients believed they were receiving röntgen therapy (treated in the röntgen therapy department in the same manner as the first group, except that they received no röntgen rays from the therapy apparatus) for three months; a third group of twenty-five patients received for three months' postural training only. The first group then received postural training for thirty days; the second group röntgen therapy for sixty days and postural training for thirty days more; the third group röntgen therapy for ninety days.

These patients were all evaluated at definite intervals and the results of these studies were compared in regard to: subjective and objective improvement with each form of treatment; the effects of each form of therapy, namely, röntgen therapy, psychotherapy, and postural therapy; improvement in relation to severity of disease; improvement in relation to duration of symptoms; improvement in relation to extension of disease; improvement in relation to radiographic changes; patient's opinion of degree of improvement due to röntgen therapy compared with objective improvement.

The results indicated immediate benefit with röntgen therapy. A report on prolonged benefit would have to await future follow-ups. The benefit was established as not being due to the psychic effect. Postural training alone could not produce as much improvement as röntgen therapy. It was concluded that the programme of treatment for rheumatoid spondylitis should include both postural and röntgen therapy.

Discussion

Dr. Roland Davison (San Francisco): We have treated a small group of these patients in San Francisco, and we too have found objective evidence of improvement following *x*-ray therapy in spondylitis. Our technique of dosage has been different from that used by Dr. Smith, and I think a little heavier. In all our patients, whether there was involvement of the sacro-iliac joint only, or also of the upper portions of the spine, we irradiated our patients, using areas, on successive days, both front and back. In other words, we were trying to give general irradiation rather than irradiation to a specific area.

I think we must ask ourselves the question why we get improvement from *x*-ray therapy in spondylitis when we get no improvement from *x*-ray therapy in patients with peripheral arthritis. We have observed some changes which perhaps have some significance. We have been studying 17-ketosteroid excretion in spondylitis as well as in straight rheumatoid arthritis in peripheral joints. In the patients with peripheral joint involvement we find no evidence of any change outside of normal levels in the excretion of 17-ketosteroids. In our patients having spondylitis we have found invariably (although our group is a small one) that where the patient has active disease there is a great increase in the ketosteroid excretion and following *x*-ray therapy the excretion is greatly reduced and brought down to normal levels. We do not know the significance of these findings as yet, and we will present it at a later time.

Dr. Richard H. Freyberg (New York): I would like to compliment the authors of this paper on the very thorough and controlled way in which they made their observations. Their results compare very favourably with those of Dr. C. J. Smyth and his collaborators in our group reported several years ago. Since that time I have had the opportunity to follow approximately 150 patients for a period sufficient to judge regarding the effects of *x*-ray therapy, and results in this larger group are similar to those we first reported.

I wish to emphasize two points: first, that to get the best results with *x*-ray therapy one has to be persistent in its use, and a sufficient amount of *x*-ray therapy needs to be given, properly planned. Some unfavourable conclusions as to effects of *x*-ray therapy, I am sure, are on the basis of inadequate treatment.

The second point is that *x*-ray therapy certainly gives quicker and better immediate results than any other form of treatment I know. It allows the patient to be comfortable while he can still conduct exercises and attempt to maintain motion in his back which, if braced or put in a cast, will very likely stiffen. I would like to crusade against the use of fixation of the back in this disease, and in favour of attempts to get results without the use of braces and casts.

Again, *x*-ray therapy, although it has been studied to determine its effects when used separately, is only one part of the programme for these patients: it is not a treatment from which adequate or best results are obtained when used alone.

Dr. W. Paul Holbrook (Tucson, Arizona): In 1929 I had the temerity to publish results in a series of these cases which gave our impression that spondylitis—as we have chosen to call it rheumatoid spondylitis—was a different disease from rheumatoid arthritis. For several years I scarcely dared show my face at these meetings. The finding has never been explained, and I call attention to it only because of this paper that has been given. Why, if rheumatoid spondylitis is the same disease as rheumatoid arthritis, does it respond to *x*-ray therapy when rheumatoid arthritis does not? Also, peripheral rheumatoid arthritis may respond to gold while spondylitis does not.

Dr. Philip Levine (Chicago): I want to compliment the authors not only for the material presented, but also for the approach they have made. Do they pay any attention to the alkaline phosphate? What is the best method of prevention of irradiation sickness? Once these patients get irradiation sickness they are almost allergic to it afterwards, so don't let them get the first attack if you can help it.

Dr. Freyberg warned us against the use of immobilization. I want to advise the use of some form of protection and support. Anybody who has treated tuberculosis of the spine knows that

you cannot immobilize a spine with any brace that has as yet been devised. But you can give them protection and support, both of which are important.

I would like to hear a few words about the vital capacity in these patients.

DR. CHARLEY J. SMYTH (Eloise, Michigan): I want to add my congratulations to the authors for an excellent, well-controlled study. I think we can all carry this sort of programme into all the work we are planning to do. One of the greatest difficulties in the whole problem of rheumatism is to try to get critical evaluation of your results. We had the temerity in the first forty-two patients we reported (I was working with Dr. Freyberg) to put a lead screen between the patient and the tube. We were not fortunate enough to be able to do as these authors have done, and segregate twenty-five patients and do practically nothing.

It is worth emphasizing that *x*-ray therapy is of no real value in any other type of rheumatic disease with the single exception of calcified, sub-deltoid bursitis. I have used it recently in a case with the so-called shoulder-hand syndrome that Dr. Steinbrocker has described. The shoulder and hand on one side were treated with three series of röntgen rays, using the same technique as Drs. Smith and Boland have described. The opposite shoulder and hand were treated with dry heat and massage daily for three months. There was absolutely no effect which could be attributed to röntgen therapy in this case.

DR. RICHARD T. SMITH (closing): The patients were very carefully leaded over the lower portion of the back, and great care was taken not to get any irradiation near the gonads. We had to spike a rumour practically every month that we were sterilizing every patient who received *x*-ray treatment, but it was well spiked. The only patient who claimed to have decreased potency was one who received psychotherapy.

The only medication we used in an attempt to prevent nausea in röntgen therapy was thiamine hydrochloride. We tried no other drugs. We have not tried testosterone. No vital capacity studies of any kind were made on these patients. We were depending upon the chest expansion as the best criteria.

DR. RALPH PEMBERTON

During the course of the meeting the President, Dr. Holbrook, introduced Dr. Ralph Pemberton, " one of the fathers of the American Rheumatism Association ". Dr. Pemberton, he said, was Chairman of the Pan-American Committee of the American Rheumatism Association, President of the Pan-American League for the Study and Control of Rheumatic Diseases, and President of the Ligue Internationale contre le Rhumatisme.

Dr. Pemberton (Philadelphia, Pennsylvania) then welcomed foreign guests as follows: " This organization is moving out into deeper waters, whether it fully realizes that fact or not, and I think we had ample evidence to-day that we are already enjoying, and benefiting by, international co-operation. In 1938 there was held in England a very brilliant Congress which a few of us attended. There was to have been a Congress in this country in 1940. The war, of course, interfered. There is expectation in a great many different directions throughout Europe and now throughout Central and South America, that we will hold another Congress at some time in the not distant future. Last night the Executive Committee decided that it would take part in an International Congress to be held here under

the auspices of the Ligue Internationale contre le Rhumatisme in 1948. If that period should prove to be too early, the year will be 1949, but it is definitely upon the agenda of this organization and we desire, therefore, at this time to make that fact known.

" You know, all of you, something of the existence of the Pan-American League for the Study and Control of Rheumatic Diseases. It has had a brief but active existence; so much so, indeed, that for the first time, I think, in the history of the study of rheumatism here, there have been a number of requests from our colleagues in the Latin Americas for places upon our programme. It is regrettable that papers accompanying these requests arrived too late for inclusion.

" We also have some visitors from Central and South America, as well as from Canada. There would have been more, I feel pretty sure, except for the railroad difficulties which exist because of the strike.

" You have already heard from Dr. Saenz of Peru. There is here Dr. Calderon, also of Peru. Dr. Adamson of Canada, President of the Canadian Rheumatic Disease Association, is here, as are also Dr. Barnhart, Secretary, and Dr. Jutrac and Dr. Gasselin, both from Canada. I have information that Dr. Brøchner-Mortenson of Denmark is here. I have had correspondence with Dr. Jarløv of Copenhagen, Denmark, and I understand that he has gone out of his way to attend this meeting. I want to assure these gentlemen on behalf of the American Rheumatism Association and on behalf of the Ligue Internationale that they will receive a very cordial welcome from us. I know of no better augury for the future of this Association than the fact that it is beginning to stimulate men elsewhere throughout other countries of the world. I hope very much, and I know you all do too, that the future will show an even closer co-operation."

ABSTRACTS

[The abstracts are divided into the following sections: acute rheumatism; articular rheumatism (rheumatoid arthritis, osteo-arthritis, spondylitis, miscellaneous); gout; non-articular rheumatism; general articles. After each subsection of abstracts follows a list of articles that have been noted but not abstracted. Not all sections may be represented in any one issue.]

Acute Rheumatism

Morphological Equivalents in Polyarthritis Rheumatica, Periarteritis Nodosa, Transient Eosinophilic Infiltration of the Lung and other Allergic Syndromes. BERGSTRAND, H. (1946). *J. Path. Bact.*, **58**, 399.

The author says that " such syndromes as polyarthitis rheumatica, periarteritis nodosa, endo-, myo-, and pericarditis rheumatica and transient lung infiltration with eosinophilia " are localized manifestations of the antigen-antibody reaction. There is, perhaps, a too ready belief in the completeness of the similarity that admittedly exists in the morbid anatomy of the hyperergic diseases. The 4 cases the author describes were clinically asthmatic, and all ended fatally. In all cases the lungs showed polyarteritis nodosa and widening of the interlobular septa, and in 3 early infiltrates, as described by Klinge in the heart in acute rheumatic disease, were present. In 2 cases the pulmonary septa showed " rheumatic granulomata ". No case had endocarditis, but 1 had a myocardial granuloma. [From the illustration this might be a later coronal Aschoff body (terminology of Gross), but there is no mention of the histological state in the region of the posterior mitral root and left auricular endocardium. The author does not state whether his cases had received treatment with sulphonamides.] *A. C. Lendrum.*

Laboratory and Clinical Criteria of Rheumatic Carditis in Children. TARAN, L. M. (1946). *J. Pediat.*, **29**, 77.

The author assesses the value of the various diagnostic criteria as a measure of continued activity in rheumatic carditis. Two hundred boys and girls of from 6 to 14 years were observed from the beginning of an attack of rheumatic carditis to the end of the active process and for at least 6 months after the end of the active period. The only treatment was good nursing, balanced diet, and moderate amounts of synthetic vitamins. Occasionally a child was given small doses of salicylates for arthralgia. In each case there was a complete clinical and laboratory examination as well as a cardiographic and immunologic investigation.

Leucocytosis.—One out of 10, no leucocytosis at all; 9 out of 10, continued leucocytosis for the first 2 weeks; 7 out of 10, continued leucocytosis at end of fourth week. At the end of 7 weeks there was no leucocytosis in any case. All cases with leucocytosis showed clinical rheumatic activity, and 9 out of 10 continued to show clinical rheumatic activity when the leucocytosis had disappeared.

Fever.—Fever was not a manifestation of cessation of rheumatic activity in this series; the average febrile period was 6 weeks.

A-V conduction.—In this series a prolonged P–R interval in a rheumatic child in the absence of other laboratory or clinical evidence was not found to be a safe index of continued rheumatic activity, and the return to a normal conduction time did not always mean cessation of activity.

Pulse rate.—This was found to be an adequate index of cessation of activity. There was no correlation between pulse rate and temperature. The rate was highest during the first 3 weeks of the disease, and was as high as 140, and no case showed a drop to below 100 before the end of the ninth week.

Sedimentation rate.—This was found not to be as reliable a guide as is commonly believed. Many cases showed a still active rheumatic condition with a normal sedimentation rate. At the end of 16 weeks a number of cases with no clinical evidence of activity had a slightly elevated sedimentation rate.

Weight gain.—This also was not found to be an index of quiescence. At the end of 7½ months all the children had reached a normal weight gain level, yet 40% still showed mild rheumatic activity.

Haemoglobin.—All cases showed a moderately severe anaemia to start with, the haemoglobin ranging from 7 to 9 g.; in 2 children it was as low as 5 g. It was only after 32 weeks that all the cases returned to 12·5 g. or more. However, 40% still showed clinical rheumatic activity after the haemoglobin was normal.

Vital capacity.—In this series vital capacity was found to be the most sensitive single index, all the children having a vital capacity of 40% or less below normal for age and body surface. None reached the normal again until 16 weeks after the onset of the carditis. This index also

failed as a specific diagnostic measurement, because some children continued to have clinical evidence of disease although the vital capacity was normal.

The relation between clinical activity and various tests is indicated in a table. The author points out that active rheumatic disease must be suspected when there is tendency to fatigue without cardiac insufficiency, or when there is emotional instability or marked pallor. Marked tachycardia with a tumultuous rhythm, and a gallop rhythm with rapid or slow cardiac rate, are looked upon as evidence of rheumatic carditis, and their absence as auscultatory evidence that carditis is at an end. However, the author finds that these criteria are inadequate in diagnosing mild smouldering carditis. Rest in bed is considered the treatment *par excellence*. *Richard Sands.*

The Effect of Salicylates on Acute Rheumatic Fever. WARREN, H. A., HIGLEY, C. S., and COOMBS, F. S. (1946). *Amer. Heart J.*, **32**, 311.

This is a study of 186 cases of rheumatic fever observed for three years. Salicylate was given according to three plans. In the first, small doses (2 to 7 g.) were given to relieve symptoms; in the second, large doses (10 to 16 g.) were given during the whole period of rheumatic activity, as judged by the sedimentation rate; lastly, a small group received intravenous salicylate (10 g. in a litre of normal saline) for one week, and then large oral doses (10 to 16 g. daily).

Large doses of salicylate were no more effective than small doses in reducing the sedimentation rate. It was found that large oral doses controlled fever more rapidly than smaller doses or intravenous medication. Large doses of the drug did not prevent the development of valvular lesions, or the progress of pre-existing cardiac damage. The authors found that pericarditis was more rapidly controlled by large-dose therapy. Large doses or intravenous therapy were no more efficacious than small does in restoring a prolonged P–R interval in the electrocardiogram to normal limits.

The authors point out that when large doses are given the signs of toxicity must be thoroughly understood and promptly recognized. Tinnitus and slight deafness are constant with doses of 10 g. daily. The earliest warning sign of toxicity is hyperpnoea, and, if this is disregarded, tetany, maniacal delirium, and loss of consciousness may occur. These symptoms promptly subside with cessation of salicylate and the administration of sodium bicarbonate. It was found that 7 to 8 g. of sodium salicylate daily in divided doses maintained a blood level of 35 to 50 mg. per 100 ml. in young adults. No bicarbonate was given with these doses, and toxic reactions rarely occurred.

Intravenous therapy offered no advantages over oral administration. It could be claimed that large amounts of salicylate early in the disease caused an early reduction in fever, which, by decreasing the heart rate, lessened the work of the heart but did not prevent heart damage. Early relief of symptoms must not be allowed to lull the patient into a sense of false security in the belief that he is cured. If he is allowed to resume normal activity at once he may suffer as much damage, or more, than if he was untreated. Sodium salicylate in any dosage does not effect a cure, and so far there is nothing in drug therapy which will obviate the need for prolonged rest and reduction of physical activity. *James W. Brown.*

The Incidence of Rheumatic Fever and Heart Disease in School Children in Dublin, Georgia, with Some Epidemiological and Sociological Observations. QUINN, R. W. (1946). *Amer. Heart J.*, **32**, 234.

In Dublin, Georgia, U.S.A., 400 school children, average age 12½ years, of whom 59% were white and 41% were coloured, were examined for evidence of previous rheumatic fever or present rheumatic heart disease. Eight children, three of them coloured, were found to have had rheumatic fever; four children, one a negro, had rheumatic heart disease. *E. B. G. Reeve.*

Clinico-Statistical Facts Concerning the Aetiological Problem of Acute Articular Rheumatism. (Rilievi clinico-statistici sul problema etiologica del reumatismo articolare acuto.) OPPENHEIM, M. (1946). *Rass. int. Clin. Terap.*, **26**, 335.

Acute Articular Rheumatism in Children. (Le rhumatisme articulaire aigu chez l'enfant.) LAPOINTE, D. (1946). *Laval méd.*, **2**, 810.

Diagnosis of Rheumatic Fever. GUY, P. F. *Northw. Med., Seattle*, **46**, 38.

Pathology of Rheumatic Fever. DREW, W. B. (1947). *Northw. Med. Seattle*, **46**, 39.

Purpuric Manifestations of Rheumatic Fever and Acute Glomerulonephritis. JONES, R. H., MOORE, W. M. (1946). *Amer. Heart J.*, **32**, 529.

Statistics of Rheumatic Fever in Mexico City. (Frecuencia de la fiebre reumatica en la ciudad de México. Estudio bioestadístico.) ROBLES GIL, J. (1946). *Arch. Inst. Cardiol. Méx*, **16**, 311.

Pneumonitis Occurring in Rheumatic Fever. GRIFFITH, G. C., PHILLIPS, A. W., and ASHER, C. (1946). *Amer. J. med. Sci.*, **212**, 22.

Articular Rheumatism

(Rheumatoid Arthritis)

Gold Treatment of Chronic Arthritis in Children. (Over Gondbehandeling Bij Chronische Arthritis Von Kenderem.) HALBERTSONA, T. J. (1946). *Mschr. Kindergeneesk.*, **10**, 297.

There is a dearth of literature on gold treatment of chronic polyarthritis in childhood. The author reports his results in 6 cases, ranging in age from 4 to 14 years. He discusses the confusing nomenclature of chronic arthritis in childhood, concludes that the term "Still's disease" should be dropped, and affirms that a condition is found in children which is in every way comparable to that of rheumatoid arthritis in adults, even in its favourable response to gold administration. The erythrocyte sedimentation rate returned to normal in all his cases after treatment; this return is taken as a criterion of cure.

"Solganal B" was used as a 2% solution in oil containing 1 mg. gold in 1 ml.; injections were given twice weekly, the dose varying between 1 and 4 mg. of gold, and a course consisted of 10 injections. Several courses with an interval between were usually given. In one case, improvement was only seen with the fourth course. No toxic reactions occurred. Two cases showed a harmless eosinophilia (up to 20%) which subsided on stopping the gold. Five patients were completely cured, and the sixth was left with some residual disability in the knee. *S. S. B. Gilder.*

Still's Disease Successfully Treated with Prostigmine. Report of Case. RITTWAGEN, M. (1946). *Arch. Pediat.*, **63**, 630.

An 11-year-old coloured girl, suffering from severe Still's disease, had been treated without success with salicylates given by mouth and intravenously, with large doses of sulphonamides, with intramuscular and intravenous penicillin, and with massive vitamin-D therapy. She also had general treatment, repeated blood transfusions, and physiotherapy. As the pain persisted it was decided to try oral and intramuscular prostigmin. She was given intramuscular injections of prostigmin methyl sulphate [the dose is given as "one ampoule, 1–2,000, three times daily"] and 15 mg. of prostigmin bromide by mouth once daily for 2 months. The intramuscular doses were then stopped, and the oral doses increased and later decreased. At the same time orthopaedic measures were taken which consisted of tenotomies and plaster splinting. The response to treatment with prostigmin was almost immediate, and after 5 months all signs of activity of the disease had disappeared and function was very good. The author discusses the manifestations and differential diagnosis of Still's disease. The patient described had had an attack of pericarditis which cleared up uneventfully. No new light was thrown on the aetiology of the condition. *W. Tegner.*

The Heart in Rheumatoid Arthritis. ROGEN, A. S. (1947). *Brit. med. J.*, **1**, 87.

The author reviews recent work on the aetiological relationships between rheumatic fever and rheumatoid arthritis, with special reference to the cardiovascular system. The cardiovascular system was examined in 33 consecutive cases of rheumatiod arthritis; 22 of the patients were females. No evidence of mitral stenosis was found. In 1 case only, a woman of 68, was there a loud apical systolic bruit which was considered to be organic; in 8 cases there was a functional murmur. The electrocardiograms of 29 patients showed no changes suggestive of rheumatic fever, though in some cases there were T-wave changes corresponding in all probability to the state of arterial degeneration occurring in old people, who formed the majority of the patients in this series. No macroscopical or histological changes of rheumatic fever were seen in the 1 case which came to necropsy.

[These results are at variance with the reports of some, but not all, workers, and serve to emphasize the limited value of comparisons between the clinical manifestations of rheumatic fever and rheumatoid arthritis in the present state of our knowledge of the rheumatic diseases.] *J. W. Brown.*

A Therapeutic Score Card for Rheumatoid Arthritis. A Standardized Method of Appraising Results of Treatment. STEINBROCKER, O., and BLAZER, A. (1946). *New Engl. J. Med.*, **235**, 501.

The authors have devised a "therapeutic score sheet" as a means of assessing the results of treatment in chronic rheumatoid arthritis. Debit marks are allotted to the chief features of rheumatoid arthritis. The total debit marks subtracted from 100 represents the patient's index number as a percentage of normal; a rise in this figure gives a measure of the patient's improvement. At the first examination each feature, even if present in slight degree, is awarded the maximum debit marks, and these are reduced at subsequent examinations if improvement has occurred. Thus, apart from the appearance of a new feature, there is no provision for recording a deterioration. The features selected are active joint swelling, sedimentation rate, articular mobility, joint tenderness, weight gain (or loss), haemoglobin, pain, well-being, and functional capacity.

Active joint swelling is debited 50 marks at the original examination. At subsequent examinations the debit may be reduced as far as 40, but never below this while any trace of active swelling remains. Active swelling must be carefully distinguished from permanent thickening of the joint. Rates of 15 mm. by the Cutler method and 25 mm. by the Westergren are taken as bases for the sedimentation rate. A rate at or above these levels requires the maximum debit of 15 marks. The debit is not increased if the rate should rise, but a proportionate reduction is made if it should fall. The other features carry a maximum debit of 5 marks each, giving a possible total of 100 debit marks. The standard haemoglobin level is taken as 80%. The authors claim that their scheme provides a set of criteria which, even if derived from different observers, gives reliable information for the evaluation of therapeutic agents.

H. F. Turney.

Rheumatoid Arthritis. I. Introduction to a Study of its Pathogenesis. WALLIS, A. D. (1946). *Amer. J. med. Sci.*, **212**, 713.

Rheumatoid Arthritis. II. Non-specific Serologic Reactions. WALLIS, A. D. (1946). *Amer. J. med. Sci.*, **212**, 716.

Rheumatoid Arthritis. III. The Pneumococcus Antibodies. WALLIS, A. D. (1946). *Amer. J. med. Sci.*, **212**, 718.

The current medical view that true rheumatoid arthritis is due to infection is open to criticism. It is based chiefly upon superficial resemblances between rheumatoid arthritis and certain infectious processes such as gonococcal arthritis. Rheumatoid arthritis has now emerged as a clinical entity distinct from other types of polyarthritis in which the causation may reasonably be inferred to be metastatic from a focus of infection, but aetiological confusion still persists. Moreover, certain serological observations have been interpreted as supporting an infective aetiology in rheumatoid arthritis. The author, who is Research Fellow in Arthritis in the University of Pennsylvania, has examined the foundations of the bacterial theory, and more specifically the haemolytic streptococcal theory, of the origin of rheumatoid arthritis, and has found them to be insecure. In his selection of material for this investigation he used only typical cases of at least a year's duration and with symmetrical involvement of the proximal interphalangeal joints of the fingers.

The general arguments against a bacterial origin which he quotes are as follows: The presence of bacteria of any species has not been consistently demonstrable in the blood of patients with rheumatoid arthritis. The extraordinary prolongation of the active stage of the joint lesions in this disease and their tendency to symmetry are arguments against bacterial aetiology in general, and their indifference to both sulphonamides and penicillin is against a streptococcal aetiology in particular. With regard to antistreptolysin and antifibrinolysin tests, these antibodies were not found in significant titre, and were never comparable with those found in cases of acute rheumatic fever or in known haemolytic streptococcal infections. The sera of many patients with well-established rheumatoid arthritis, moreover, have a tendency to precipitate in the saline control tube of a precipitin test, especially after centrifugalization. He points out that many rheumatoid arthritis sera also differ from the normal in being able to agglutinate suspensions of fine collodion particles. From these observations he concludes that supposedly specific reactions in which the serum of patients with rheumatoid arthritis takes part should be interpreted with considerable caution.

Following on these findings, and apparently dependent on them, the author found that the sera of patients with rheumatoid arthritis will precipitate the somatic carbohydrate of the pneumococcus a little more strongly than does the serum of non-arthritics. In the same way the rheumatoid serum also agglutinates non-encapsulated pneumococci a little more strongly. He explains these findings as being due to a non-specific enhancement of the action of normally present antibodies to Gram-positive cocci of many types. He considers: (1) that the importance of the distinction between true rheumatoid arthritis and arthritis of other types, particularly that which is secondary to a focus of infection, is of great importance; (2) that the foundations of the bacterial theory, and more specifically the haemolytic streptococcal theory, of causation of true rheumatoid arthritis are insecure; (3) that supposedly specific reactions in which serum from patients with rheumatoid arthritis is employed should be suspect; and (4) that the increased ability of such serum to agglutinate other Gram-positive cocci, such as the pneumococcus, appears to be due to a non-specific increase in the action of normally present antibodies.

W. S. C. Copeman.

Physical Medicine in the Treatment of Arthritis. KESSLER, H. (1947). *N.Y. St. J. Med.*, **47**, 1244.

Clinical Study of Subcutaneous Rheumatic Nodules in Rheumatoid Arthritis. (Estudo clinico dos nodulos reumaticos subcutaneous da artrite reumatoide.) LUCCHESI, M. and O. (1946). *Bol. Liga argent. Reum.*, **9**, 129.

(Spondylitis)

A Rare Cause of Dysphagia: Cervical Spondylytis. (Une cause rare de dysphagie: La spondylose cervicale.) POINSO, R., and CHARPIN, J. (1946). *Rev. Rhum.*, **13**, 327.

A man, aged 47, suffered for 18 months from ankylosing polyarthritis, probably of tuberculous origin, with involvement of most joints and also the spine. He had noticed difficulty in swallowing solid food, and located the obstruction at the root of the neck. Radiological examination of the spine showed decalcification of the vertebral bodies, with numerous osteophytes bridging the intervertebral spaces, especially between the second and third and the fifth and sixth cervical vertebrae. At the latter level a rather large, partially calcified projection 6 to 7 cm. in height spread out in front of the spine. There was no continuous calcification of the anterior vertebral ligament. Other possible causes of dysphagia were excluded, and after discussing the part played by spasm the authors conclude that in their patient the dysphagia was due to direct compression of the pharynx by the vertebral osteophytes. *T. G. Reah.*

Rheumatic Perispondylitis of the Cervical Spine and the Cervical Syndrome. (Dierheumatische Perispondylitis der Halswirbelsäule und das Zervikalsyndrom.) BELART, W. (1946). *Schweiz. med. Wschr.*, **76**, 797.

A common clinical syndrome, which often ends in cervical spondylosis, is described, and named " the cervical syndrome ". The prominent symptom is the presence of paraesthesiae in the hands, coming on characteristically in the early hours of the morning. It is accompanied by neuralgic pains in the arms, especially in those whose work involves a fixed position of the neck in flexion, as in typing or sewing. Pain is felt at the deltoid insertion, and at the epicondylar origin of the extensor muscles of the forearm. Later there is a painful stiffness of the neck, and pain radiating from the nape to the occipital region and the shoulders. Systemic symptoms, such as anginoid pain, mental torpor and irritability, and, rarely, complaints of choking or difficulty in swallowing, may be associated. In the later stages there are cervical crepitus and radiological evidence of spondylosis. Chronic pharyngitis and tonsillitis are practically constant associations.

[Arguments are advanced supporting the hypothesis that this syndrome is caused by a rheumatic inflammation of the soft tissues of the spine—a perispondylitis, the end-result of which is a spondylosis. It is pointed out that symptoms appear long before there is radiological evidence of osteophyte formation, and, therefore, the suggestion that symptoms are due to the mechanical pressure of osteophytes on cervical nerves is regarded as untenable. It is presumed that the inflammatory oedema provokes disturbances in the adjacent sympathetic nerves, with ensuing vasomotor disorder responsible for the numbness and paraesthesiae of the hands. The aetiology is discussed, and attention directed to the associated pharyngitis and tonsillitis. It is suggested that there may be a direct spread of infection by lymphatics from the pharynx to the adjacent soft tissues of the cervical spine. The possibility is suggested of a causal relation between this condition and spondylosis, muscular rheumatism, neuritis, neuralgia, osteoporosis of the spine, chronic meningitis, and vegetative disturbances.] *Kenneth Stone.*

(Miscellaneous)

Reiter's Disease with Prolonged Auriculo-Ventricular Conduction. FEIRING, W. (1946). *Ann. intern. Med.*, **25**, 498.

Two cases of Reiter's syndrome (polyarthritis, urethritis, and conjunctivitis) are described in which serial electrocardiograms revealed transient prolongation of the P–R interval from 0·18 and 0·19 seconds respectively to 0·24 seconds. The heart appeared otherwise normal, although a faint localized apical systolic murmur was heard in both. There was no evidence of preceding pyogenic infection in case 1; but there had been a series of infective incidents in case 2, the last (cellulitis of the calf requiring incision and drainage) beginning five and a half weeks before the first manifestation of Reiter's syndrome (urethritis), and nine weeks before the onset of polyarthritis. The significance of the prolonged P–R interval is doubtful. *Paul Wood.*

Reiter's Disease. BAXTER, C. R. (1946). *Brit med. J.*, **2**, 858.

The author records a case of Reiter's disease in a soldier of 41 years who, while serving overseas in August, 1945, developed purulent conjunctivitis. The next month, on repatriation, in addition to the active conjunctivitis, which was still present, he had a purulent urethral discharge which did not contain gonococci. Serological examinations were likewise negative. Parenteral penicillin (dose unspecified) led to the disappearance of the discharge within 5 days. Two months later, however, there occurred in the right eye an intraocular haemorrhage followed by iritis which ran a course of 10 or 12 weeks. Stiffness of the ankles, knees, and shoulders then occurred and, 2 weeks later, swelling of the second left metacarpo-phalangeal joint, associated for the first time with a pyrexia and a scaly eruption of the soles.

In December, 1945, the patient was admitted to hospital under the care of the author, when,

in addition to the above, he had painful swollen ankles; stiff, painful, but not swollen knees, left shoulder, and elbow; and slight bilateral conjunctivitis. There was no iritis, urethral discharge, or pyrexia, and the routine serological tests were normal apart from the erythrocyte sedimentation rate, which was 106 mm. in 1 hour. Nineteen days after admission a "course" of myocrisin was started, and this was followed by a slow but steady improvement of the polyarthritis, the patient being able to walk within 2 months and having no subsequent relapse after a follow-up of 10 months. A month after starting gold therapy, however, there was a relapse of the iritis, which resolved during 10 weeks of local therapy, to be followed in May, 1946, by iritis in the left eye, which similarly disappeared in about 8 weeks. During the first 12 weeks there was an irregular pyrexia never exceeding 98·8° F., while the keratodermia blennorrhagica of the soles resolved *pari passu* with the joint lesions.

[No mention is made of the existence or otherwise of balanitis circinata sicca, the actual amounts of gold salts employed, or the subsequent behaviour of the erythrocyte sedimentation rate. Fever therapy would probably have considerably shortened the duration of the iritis, though the possibility of a slow but steady response to gold salts is in accord with the findings of other workers even if doubt is expressed in the summary whether the gold has exerted any specific effect.]

R. R. Willcox.

A Further Report of an Epidemic of Acute Polyarthritis. GOSWELL, G. (1946). *Med. J. Austral.*, **2**, 861.

An epidemic is reported, in a Royal Australian Air Force unit stationed in Australia, of a mild acute polyarthritis associated with lymphadenitis and a transient exanthem. Three similar outbreaks had occurred previously in the same area. The report gives a detailed account of the clinical features of 51 cases. Illness was mild, with little or no malaise, and with pyrexia only in the more severe cases; 16 required in-patient treatment. The duration ranged from a few days to several weeks; more than half of those affected had completely recovered by the seventh day. A dull aching and a feeling of stiffness in several joints were the initial symptoms. Pain had abated within 4 or 5 days; residual stiffness quickly responded to exercise, leaving no joint sequelae. In the first few days joints were tender, but in only 15 cases was there any swelling from synovial or periarticular effusion. Tender enlarged lymph nodes, especially in the axillae and inguinal regions, were usual. A generalized papular rash was observed in 3 cases, beginning 24 to 48 hours after the onset and disappearing by the fourth day. Twelve patients had pyrexia for 4 to 6 days, temperatures usually ranging from 99·6° to 100·6° F. On clinical grounds it was thought possible to exclude a dysenteric arthritis, the joint manifestations of dengue, acute rheumatism, and rheumatoid arthritis. Laboratory investigation of the epidemic was not practicable. *Kenneth Stone.*

Heberden's Nodes. Their Relation to other Degenerative Joint Diseases. STECHER, R. M. (1946). *Arch. phys. Med.*, **27**, 409.

A series of 94 women with Heberden's nodes were investigated to discover what proportion had noteworthy degenerative disease of other joints, and to make a comparison with degenerative disease in a control group of 109 patients with no familial history of nodes. The investigated group had an average age of 59·7 years, with individuals ranging in age from 36 to 76, while the control group had an average age of 55·9 years, with individuals ranging in age from 32 to 77. Of the women with Heberden's nodes, 12 (12·6%) were found to have degenerative joint disease, 11 in one knee and 1 in a hip, the disease in no instances being severe enough to incapacitate the patient. In 19 other patients who complained of "arthritis and rheumatism", and who resorted to acetylsalicylic acid for relief, there were no objective signs to warrant a clinical diagnosis of degenerative joint disease. Crepitus as a sign was noted in 34 cases (36%) and was looked on as abnormal but in itself not sufficient for a diagnosis of degenerative joint disease. It was not a forerunner of future disease. Its significance in these cases was not clear. In the control series of 109, only 3 had definite degenerative joint disease, 25 (23%) had joint crepitus, and the others appeared to be free from disease.

The author states that Heberden's nodes are a particular form of degenerative arthritis, the incidence of which is influenced by age, sex, and race, and that heredity is the most important single factor, the condition being dominant in the female and recessive in the male. Genetically the theoretical incidence in the female is 10 times greater than in the male, and this corresponds with an observed incidence of 3% in a male group and 28% in a female. Heberden's nodes are to be regarded as a form of osteo-arthritis, since degenerative changes in other joints occur 6 times more frequently in these patients than in the control series. The presence of the nodes betokens an increased susceptibility to degenerative joint disease. *Richard Sands.*

Benzyl-imidazoline in Anti-rheumatic Therapy. (La benzyl-imidazoline en therapeutique anti-rhumatismale.) COSTE, F., and HOCHFELD, M. (1947). *Sem. Hôp., Paris*, **27**, 325.

Gout

Gouty Rheumatism. (Rhumatisme goutteux.) HEINSINS, D. J. van B. (1946). *Geneesk. Gids.*, **24**, 359.

The manifestations of rheumatism and gout occur together more often than is generally supposed. The name "rhumatisme goutteux" is used provisionally to denote this combination. The diagnosis of this condition is important; many cases of atypical gout are diagnosed as rheumatic and given entirely inappropriate treatment. Points in differential diagnosis, which may be extremely difficult, are the greater likelihood of a family history of arthritis and of signs of arteriosclerosis in gout, while a study of the blood chemistry and of radiographs may help. Gout attacks the male more frequently, and the pain is more intense than in rheumatism, but the gouty individual, apart from his attacks, is of a more cheerful disposition. Lastly, the effect of colchicum should be tried. The author has used Umber's test by giving an intravenous injection of 500 mg. of uric acid with 1 g. of piperazine dissolved in 40 ml. of physiological saline. In the normal subject, the uric acid level in the blood falls to its pre-injection figure within 24 hours. *S. S. B. Gilder.*

Non-Articular Rheumatism

Physiotherapy in Peri-arthritis of the Shoulder. (Indications et résultats de la physiothérapie dans les syndromes périarthritiques de l'épaule.) BOIJEAU, A., and NAUDIN, E. (1946). *J. Radiol. Électrol.*, **27**, 247.

The aetiology of the so-called peri-arthritic syndromes of the shoulder varies. In 70 out of 100 cases observed by the authors the primary cause was a fibrotic sclerosis of the subacromial and subdeltoid bursae. This condition is usually painless. Peri-articular calcifications are relatively rare, while tenosynovitis, particularly of the long head of the biceps, is met with in about 20% of cases. This last condition, which is the most painful, usually improves spontaneously in a few weeks or months, while the most obstinate cases are those which show peri-articular calcification.

The radiographic examination is negative in about 70% of cases. Peri-articular calcification accounts for 5%. In 17% the head of the humerus presents a typical "hatchet" deformity, while the remaining 8% show either changes produced by a previous trauma or localized decalcification of the humeral head, mainly in the lesser tuberosity, or signs of a chronic acromioclavicular arthritis.

Of the various treatments recommended, massage is particularly useful in cases of synovitis and peri-articular calcification. Infiltration analgesia affords only temporary relief. Short-wave diathermy has proved disappointing, while infra-red treatment seems to be generally soothing. Radiotherapy was successful in the majority of cases. The pain is relieved by about five daily doses of 50–100 *r* of semi-deep rays (150 kV, 5 mm. aluminium filter). In ankylosing peri-arthritis the author advises 8 weekly treatments of 200 *r* each of a similar radiation, given alternatively to the front and back of the joint. *A. Orley.*

Rheumatic Polytendovaginitis. (Polytendovaginitis rheumatica.) BAUMGARTNER, W. (1946). *Schweiz. med. Wschr.*, **76**, 809.

It is known that the tendon sheaths can be affected in the course of both acute rheumatism and chronic polyarthritis. But there is little information in the literature about "tendovaginitis rheumatica", where tendon sheaths rather than joints seem to take the impact of the disease process. Clinical notes of 2 cases are recorded. In the first the development of pancarditis and rheumatic nodules made it probable that the disease process was rheumatic in nature. A girl of 15 developed a painful swelling on the palmar aspect of both wrists, and fleeting joint pains. Some nine months later there was still free movement in all the joints, on the palmar aspect of each wrist was a circumscribed soft swelling the size of a plum, connected with the flexor sheaths, and there were similar swellings in the peroneal tendon sheaths below the lateral malleolus. Biopsy showed a chronic tendovaginitis with no specific features and no appearance of tuberculous infection. Cultures were sterile. During the next four months typical subcutaneous rheumatic nodules developed. The erythrocyte sedimentation rate was 48 mm. in the first hour, later increasing to 95 mm. Haemoglobin was 70%, and the white cell count 4,000 per c.mm. The girl showed evidence of a deficiency of the sex hormones. Pericarditis and endocarditis developed later. The second case was one of primary chronic polyarthritis in a patient aged 28, which began with symmetrical tendon-sheath swellings on the palmar and dorsal aspects of the wrists. Biopsy eliminated tuberculous infection, and showed the histological characters of a non-specific granulation tissue. With spread of the articular manifestations the swellings abated.

Chronic polytendovaginitis was first described in 1913. Mostly symmetrical, circumscribed painful swellings develop in tendon sheaths of hands and feet, often containing a sterile serous exudate. The process is slow and progressive, at times with acute exacerbations. Aggravation with menstruation and retrogression in pregnancy, have been noted. Occasionally bursae are affected. Histologically rheumatic polytendovaginitis shows an infiltration with lymphocytes in groups comparable

to Aschoff's nodes. In chronic cases there is an extensive proliferation of the tendon-sheath synovial villi, often accompanied by fat deposits, amounting in the final stages to a lipomatous growth. Polytendovaginitis associated in 4 cases with acute rheumatism was recorded in 1925. The tendon sheaths may be affected in Still's disease. Mayerhofer (*Ann. Pediatr.*, 1944, **163**, 169) described a case which began with inflammation of the tendon sheaths and bursae and progressed to the classical picture of Still's disease. There seems to be a counterpart in the tendon-sheath lesions of intermittent hydrarthrosis ; recurrent swelling of the extensor tendon sheaths of the fingers has been recorded in a case of angioneurotic oedema. The differential diagnosis is from tuberculous infection; from the acute tendovaginitis of gonococcal infections, which may persist in chronic form; from the common tendovaginitis stenosa crepitans, localized, and generally arising from unusual exertion; from the suppurative tendovaginitis of infected neighbouring injuries; and from the acute tendovaginitis of gout. Affection of the tendon sheaths has also been observed in lead poisoning and in dysentery.

Kenneth Stone.

Acroparaesthesia. Arthritis of the Shoulder and Brachial Plexus, and Acroparaesthesia of the Upper Limb. (Acroparestesia. La artritis de hombro, el plexobraquial y la acroparestesia de miembro superior.) OBARRIO, J. M. (1946). *Rev. Asoc. méd. argent.*, **60**, 557.

The author describes the different views which have been held about the aetiology and pathogenesis of acroparaesthesiae. He emphasizes that in many cases sleep either precipitates or aggravates the paraesthesiae, and distinguishes three forms: a diurnal form in which paraesthesiae are present throughout the day; a post-hypnotic form in which the patient is awakened by the paraesthesiae after a period of sleep usually lasting between 2½ and 4½ hours, the symptom completely disappearing after some time; and a mixed form in which paraesthesiae of minor severity are present throughout the day and are increased in intensity on waking, gradually diminishing in severity until they reach their diurnal grade. The abnormal sensation is a primary symptom, which may or may not be associated with motor, vasomotor, and (rarely) trophic disturbances. A full account is given of 3 cases (1 case of tabes, 1 of suprasellar tumour with marked fluctuations of weight, and 1 of gout, the last patient being the author himself) in order to substantiate the author's view that acroparaesthesiae in the upper limb are due to arthritis in the scapulo-humeral joint. The diagnosis of arthritis is based on the presence of crepitations over the joint (and in 1 case pain on movements); a radiological examination of the joint is reported only in Case 1, in which it was found normal. The view is put forward that the arthritis produces a neuritis in the nerves (circumflex and suprascapular) supplying the joint, which spreads to the brachial plexus, resulting in a neuritis of other nerves of the plexus and thus in the acroparaesthesiae. The fact that the condition is precipitated or aggravated by sleep is attributed to the accumulation during sleep of metabolites, particularly carbon dioxide and products of auto-intoxication from the intestines, which after waking are eliminated; this would account for the disappearance or diminution in intensity of the symptoms after waking.

[It is difficult to accept these views as an explanation. The existence of arthritis seems as little proved as the role of metabolites.]

A. Schott.

The Basis of Clinical Diagnosis of Sciatica Caused by Root Lesions of L5 and S1. (Sciatiques radiculaires L5 and sciatiques radiculaires S1.—Les fondements d'un diagnostic clinique.) DE SÈZE, S., GUILLAUME, J., and BOULARD, P. (1946). *Bull. Soc. méd. Hôp., Paris*, **62**, 347.

The authors consider that the advantages of exact location of disc and root lesions by intrathecal injection of lipiodol are outweighed by the disadvantages, such as pain and encystment of the oil. Possible alternatives discussed are the use of " pantopaque ", which is difficult to remove afterwards, and " abrodil ", which requires a preliminary spinal analgesic. Therefore they consider that the ideal method is to determine the level of the lesion from clinical examination. Straight *x*-ray photographs centred over discs L4 and L5 and L5 and S1 are also of value.

The conclusion is reached that by consideration of the state of the ankle-jerk, the distribution of sensory disturbances, the production of pain on pressure, and the appearances on direct radiography, it is possible to determine which is the affected disc in 90 to 95% of cases, without recourse to lipiodol. In the doubtful cases the authors prefer to explore both the fourth and fifth lumbar spaces, without laminectomy.

[Most of the conclusions reached will be already familiar to readers in this country, but it must be remembered that they will be new to many French readers, who have been isolated from British, American, and Swedish work during the war.] *E. G. Sita-Lumsden.*

Pathologic Intervertebral Disk and its Consequences. A Contribution to the Cause and Treatment of Chronic Pain Low in the Back and to the Subject of Herniating Intervertebral Disk. HYNDMAN, O. R. (1946). *Arch. Surg.*, **53**, 247.

General Articles

A Case of Relapsing Rheumatism ("Rheumatisme Palindromique"). (Een geval van rheumatisme palindromique.) VAN HEUSDEN, E. G. (1946). *Ned. Tijdschr. Geneesk.*, **90**, 1566.

This rare syndrome is characterized by rapid swelling of joints, which become red and painful, with restriction of movements. The attacks last a short time, sometimes a few hours only, sometimes a day or a week. Different joints are affected, either simultaneously or shortly after one another, sometimes within hours but mostly after one or several days. The joints themselves, as well as the periarticular tissues, are swollen. General symptoms, including fever, are absent. Those affected are usually under 40. The attacks may be numerous and at intervals of days or months. The joints most often attacked are those of the fingers, but the wrist, elbow, shoulder, and knee may be involved. The E.S.R. is increased (average, 30 mm. after 1 hour). There is relative lymphocytosis, but no eosinophilia or change in the blood chemistry. The *x*-ray picture is normal. The aetiology is unknown.

The present author's patient conformed to this description, although his age was 50. The joints, which were red, painful, and stiff, were attacked within a few days of each other, in the following order; the second, fourth, and third fingers, and the wrist of the left hand. In any particular joint the lesion lasted one or two days only. The E.S.R. was 35 mm. after one hour. The blood count showed 7,000 leucocytes per c.mm., of which 38% were lymphocytes. There were no eosinophils; the blood uric acid was normal, and *x*-ray examination negative. The attacks stopped after large doses of pyramidon and short-wave treatment. *R. Salm.*

Studies on Neuromuscular Dysfunction. VIII. Use of Curare to Differentiate Muscle Spasm from Organic Changes in Limitation of Passive Motion at Joints. JONES, C. W., LECOMPTE, B., KABAT, H. (1946). *South. med. J.*, **39**, 799.

This paper describes the results of intravenous injection of curare in 17 patients with limitation of joint movements; the primary object was to determine what part muscle spasm played in these cases. An initial injection of 20 to 50 mg. of "intocostrin" was followed by further small injections until the patient was unable to lift his head from the table and the hand grip was weak; in most cases a total dosage of 100 mg. was given. With this dosage, objective interference with respiration was not observed; the patients felt dizzy and had ptosis and strabismus. In 11 patients the joint stiffness was a sequel of fracture of neighbouring bones; the other patients suffered from arthritis (3), spastic palsy, contracture following burns, and recurrent dislocation. In 8 of the 17 patients, increase in the range of movement occurred with curare; 7 who showed improvement were in the fracture group, and the remaining 1 had a spastic palsy. In those patients in which curare increased the range of movement there was relief of pain, confirming the view that muscle spasm can cause pain. It is suggested that patients whose response to curare shows that spasm is present are likely to respond well to physiotherapy. In 5 cases the increased movement with curare was still present a week after the injection; to explain this the authors say: "It appears possible that the muscle spasm, once initiated, perpetuates itself by discharging afferent proprioceptive impulses which reflexly maintain the spasm in a vicious cycle". [They do not mention the possibility that the patient will permit a fuller range of passive movement once it has been demonstrated to him that such movement can occur painlessly.] *D. A. K. Black.*

Physiological Rest, with Special Reference to Arthritis and Nerve Lesions and to the Manufacture of Appliances. CAPENER, N. (1946). *Brit. med. J.*, **2**, 761.

The modern conception of physiological rest, as originally taught by Hylton and Hugh Owen Thomas, is brought up to date. The author has added some ingenious modifications to various treatments in physiological position of arthritic joints and peripheral nerve injuries. There is a table showing the optimal positions for the treatment of arthritic joints—positions which must also be suitable for ankylosis if necessary. He pleads for standardization of orthopaedic appliances in order to decrease their cost. [This article should be read *in extenso* by all interested in arthritis, particularly if they are not so well acquainted with the details of splintage as are most orthopaedic surgeons.] *V. H. Ellis.*

Bone Atrophy, Decalcification, and the Fate of the Eliminated Calcium. (Beenatrophie, decalcificatie en het lot van de hierbij vrijkomende kalk.) LUBBERHUIZEN, H. W. (1946). *Ned. Tijdschr. Geneesk.*, **90**, 950.

The process of decalcification of bone in disease is discussed, and the fate of the lost calcium speculated on. Apart from parathyroid influence and the possible effect of alterations in acid-base equilibrium, hyperaemia is considered important among causes of decalcification. Infection and trauma produce a reflex hyperaemia of bone and consequent loss of calcium.

This calcium may be eliminated from the body in the urine and may also appear in the skin, for example, in sclerodermia. Or it may be retained, as in the chronic rheumatic diseases. Osteoclasts may be involved in its removal, or a simple osteolysis may occur without their intervention. If the calcium is retained it may be deposited afresh in the tissues near the bone, e.g. the deposition in cartilage in osteochondromatosis; in the cruciate ligament in knee injuries; in bursae such as the subacomial bursa, giving rise to pain and stiffness. The author considers that the calcium deposited in the ligaments in spondylitis comes from the decalcified vertebrae. *S. S. B. Gilder.*

Subcutaneous Nodules. (Hypodermites nodulaires variables.) GOUGEROT, H., BURNIER, R., BLUM, P., CARTEAUD, —., and DUPERRAT, —. (1946). *Ann. Derm. Syph. Paris*, **6**, 381.

Three patients are described who had variable subcutaneous nodules. The first, a chauffeur aged 32, complained of pain in the lower limbs and hard painful nodules under the skin for four years. The pain was in the joints and had been intermittent. On one occasion the ankles had swollen, and once there had been fever. The nodules had varied from 10 to 30 mm. in diameter; occasionally the skin had been red over them. Clinically they resembled the Darier-Roussy type of sarcoid. The patient was pale, thin, and feverish. The tuberculin reaction (1 in 1,000) was positive. Skiagrams of the bones, joints, and chest appeared normal. Histologically, a nodule consisted of an infiltration of large epithelioid cells partly grouped in foci confined to the subcutaneous fat with fibrous bands in one part and a medium-sized vein containing an old organized thrombus in another part. The appearance was that of a sarcoid developing around a thrombosing phlebitis. Three of the six nodules disappeared soon after the biopsy. Eight new nodules were then seen. He was given large doses of vitamin D but more nodules continued to appear. Later he became clear of nodules but continued to complain of fatigue, dyspepsia, and headache.

A man, aged 54, had had two nodules on his left knee—one for four months, and one for two months. They were subcutaneous, hard, and painless; the skin over one was violet and over the other of normal colour. There was a third nodule on his right arm. His general conditions was excellent. The tuberculin reaction was strongly positive and the blood count normal. Biopsy showed an inflammatory infiltration of the subcutaneous tissue, mostly but not entirely focal. The cells were epithelioid with a border of lymphocytes at the periphery and a very few giant cells. There were no vascular lesions. The appearance was of a subcutaneous sarcoid resembling Schaumann's disease. Three weeks after the biopsy all the lesions had disappeared.

A woman aged 42, had had a basal-cell carcinoma of the nose for three years, during which time she had had pale red nodules 5 to 15 mm. in diameter on the medial aspect of her thighs. The nodules lasted a week or longer and new ones kept appearing. The Wassermann reaction and the tuberculin reaction (1 in 1,000) were strongly positive. She had albuminuria without casts. Biopsy revealed interstitial oedema in the corium. In the subcutaneous fat were foci of histiocytes and lymphocytes but no epithelioid or plasma cells. The foci were found around thrombosed veins. She was given intravenous injections of mercury cyanide and the albuminuria decreased but the nodules remained unchanged. It is suggested that the nodules were manifestations of an allergic reaction to an unascertained antigen.

E. Lipman-Cohen.

Cervical and Thoracic Intervertebral Disk Disease. YOUNG, J. H. (1946). *Med. J. Austral.*, **2**, 833.

Brachial neuritis and fibrositis should not be lightly diagnosed as causes of cervicobrachial pain. More attention should be focused on the cervical intervertebral disc as the agent responsible.

Cervical pain, acute, subacute, or chronic, intermittent or continuous, is a constant symptom; stiffness of the cervical spine, with increased pain on lateral flexion towards the affected side in herniation and away from the affected side in rupture of the disc, is a prominent feature. Localized tenderness over the affected interspace is an important sign, especially in degeneration of the disc; the best method of eliciting the sign, according to the author, is with the patient lying prone with his arms by his side, his chest supported on a pillow, and his cervical spine flexed. Symtoms of nerve-root involvement may be found in all three conditions, but more commonly in degeneration and herniation than in rupture of the disc; there may be referred pain along a part or the whole of the root distribution, tingling and numbness, some loss of pain and touch sense, and diminished or absent reflexes.

Treatment should be conservative, at least at first; on rare occasions only is there any need for operative interference.

The lesions in thoracic intervertebral disc disease are similar to those affecting cervical discs but are not so common. The greatest incidence was found at the junction of the fixed thoracic portion with the more mobile lumbar spine (D 10 to D 12), the eleventh thoracic disc being most frequently affected. The symptoms are comparable to those of cervical disc lesions.

Treatment consists of relief of pain and avoidance of strain; the comparative immobility of the thoracic spine is reinforced by the wearing of a spinal brace [for how long is not

mentioned]. However, 4 patients have been submitted to operation, 3 with degenerate discs and 1 with a herniated disc. In 2 there have been excellent results; the remaining 2 have been operated upon too recently for assessment.

David Trevor.

The Importance of Rheumatic Disease in Sweden. (Rheumatismens betydelse som folksjukdom i Sverige enligt under sommaren 1944–1945 utförd fältundersökning av befolkningen inom vissa district av landet.) EDSTRÖM, G. (1946). *Upsala Läk Fören. Forh.*, **51**, 337.

In 1943 the author carried out some investigations on the frequency of rheumatic diseases in Sweden (*Upsala LäkFören. Forh.*, **49**, 303). The present paper refers to further investigations carried out in 1944 and 1945, and gives a summary of the results. Altogether 72,000 persons were investigated, one-half from rural districts and the other half from villages. In coastal districts rheumatic fever and rheumatoid arthritis were found to be more common and more malignant than in the inland districts; this difference was, however, more pronounced in the rural districts than in the villages. The author's explanation is that the climate is the decisive factor. A seasonal difference, too, was observed, the greatest frequency occurring in winter and spring. No climatological and seasonal variations were observed in cases of sciatica and osteo-arthritis. Sciatica was found to have the same incidence in all districts; osteo-arthritis was more common in rural than in urban parts. Among the total number investigated 5,679 cases of rheumatic disease were found—that is, 7·9%. At the time of investigation the disease was active in 2,945 cases (3·8%). Permanent incapacitations from rheumatic disease numbered 6·66 per 1,000 of all cases investigated; the number of permanently incapacitated persons in the whole of Sweden, therefore, amounts to about 42,000.

F. K. Kessel.

Comparative Study of Some Better-known Classifications of Rheumatism. (Estudio comparativo de algunas de las classificaciones mas conocidas sobre reumatismo.) BUSTAMANTE, F. (1946). *Bol. Liga argent. Reum.*, **9**, 177.

OBITUARY

Dr. Sydney Monckton Copeman, who recently passed away at the ripe age of 85, had a distinguished career in the sphere of public health. Qualifying in 1885, he became a medical officer of the Local Government Board in 1891, and in that capacity did most valuable work in epidemiology, notably in the study of vaccinia and variola. His researches into the bacteriological purification of calf lymph, embodied in the Milroy Lectures in 1898, led to the adoption of glycerinated calf lymph in lieu of arm-to-arm vaccination in this country and many others, rendering vaccination a much safer and simpler operation ; with this reform his name must always be associated.

An efficient administrator, he did not neglect the laboratory, and in 1903 he received the highest honour in the scientific world when he was elected a Fellow of the Royal Society. This and many other distinctions which marked his career have been fully set out elsewhere. His interest in the problems of epidemiology was also shown by his advocacy of immunization against diphtheria, in which he was an early pioneer.

When he retired from the Ministry of Health in 1925 he devoted himself to the affairs of local government, and served for many years on the London County Council and the Hampstead Borough Council, where his knowledge of public health was of the greatest value.

His wide culture, tact, and courtesy, and his generous hospitality, gained him a circle of friends among whom his memory will not soon be forgotten. Although rheumatology did not come within the scope of his generally recognized activities, he was an honorary life member of the Empire Rheumatism Council, and he may be credited with keen interest in the subject since his son, Dr. W. S. C. Copeman, has done and is doing such important work in this sphere and has evidently inherited many of the qualities of his distinguished parent. To him the sympathy of readers of the *Annals* will be generally accorded.